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(54)【発明の名称】　経皮治療用装置

(57)【要約】
【課題】本発明は装置の保存中に、薬剤との相互作用による付着性の低下、及び感圧性接着剤層を周囲に配責することによるかさばりに伴う皮膚刺激の増加をなくすことなどを目的としている。
【解決手段】本発明は、
（Ａ）　薬剤非透過性の裏打ち材層
（Ｂ）　裏打ち材層と薬剤放出層との間に、治療に有効な量の薬物が含有された薬剤貯蔵層、
（Ｃ）　薬物の放出をコントロールし得る感圧性接着剤層からなる薬剤放出層、よりなる少なくとも３個の層を有する経皮治療用装置に関する。

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【特許請求の範囲】

【請求項１】　（Ａ）　薬剤非透過性の裏打ち材層

（Ｂ）　裏打ち材層と薬剤放出層との間に、治療に有効な量の薬物が含有された薬剤貯蔵層、

（Ｃ）　薬物の放出をコントロールし得る感圧性接着剤層からなる薬剤放出層、よりなる少なくとも３個の層を有する経皮治療用装置。

【請求項２】薬剤放出層の外側に、装置の使用に際して剥離することが可能な剥離ライナー層を有する請求項１に記載の経皮治療用装置。

【請求項３】薬剤の放出をコントロールする薬剤放出層が、薬剤透過性フィルム及び感圧性接着剤層からなる請求項１又は２に記載の経皮治療用装置。

【請求項４】感圧性接着剤層がゴムエラストマー、粘着付与樹脂、並びに、軟化剤及び／又はアクリル系粘着剤が配合されてなる請求項１、２又は３に記載の経皮治療用装置。

【請求項５】感圧性接着剤層が、感圧性接着剤層全重量に対して、ゴムエラストマーが５～５０重量%、粘着付与樹脂が５～５０重量%、軟化剤が１０～７０重量%、アクリル系粘着剤が０～８０重量%である請求項４に記載の経皮治療用装置。

【請求項６】薬剤透過性フィルムが通気性を有する微多孔性フィルム状、紙状、布状、又は、スポンジ状の高分子の１種又は２種以上からなる請求項３～５のいずれか１項に記載の経皮治療用装置。

【請求項７】薬物が卵胞ホルモン及び／又は黄体ホルモンである請求項１～６のいずれか１項に記載の経皮治療用装置。

【請求項８】卵胞ホルモンがエストラジオール、エストロン、エストリオール、エキリン、エキレニンまたはそれらの誘導体からなり、黄体ホルモンがプロゲステロン、カプロン酸ピドロキシプロゲステロン、酢酸メドロキシプロゲステロン、ジドロゲステロン、酢酸クロルマジノン、エチステロン、ジメチステロン、ノルエチステロン、酢酸ノルエチステロン、エナント酸ノルエチステロン、酢酸エチノジオール、酢酸メゲストロール、アリルエストレノールまたはそれらの誘導体からなる、１種又は２種以上である請求項７に記載の経皮治療用装置。

【請求項９】薬剤が低級アルコール、保湿剤、水、刺激低減剤及び吸収促進剤を含有してなる請求項１～８のいずれか１項に記載の経皮治療用装置。

【請求項１０】薬剤が低級アルコールが１０～４０重量%、保湿剤が２０～４０重量%、水が２０～７０重量%、刺激低減剤が１～１０重量%、吸収促進剤０．１～１０重量%を含有してなる請求項９に記載の経皮治療用装置。

【発明の詳細な説明】

【０００１】

【発明の属する技術分野】本発明は経皮薬物治療の分野

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に関する。より詳細には薬物放出面に薬剤放出コントロール感圧性接着剤を積層することにより装置の保存中における液状薬剤の薬物貯蔵槽からの漏出を抑制することを可能にした経皮治療用装置であって予定量の薬剤を正確かつ確実に患者に適用できることを特徴とする経皮治療用装置に関するものである。

【０００２】

【従来の技術】現在すでに経皮治療の分野においてはエストラダーム（商品名）、ニトロダーム（商品名）などの経皮治療用装置が開発され販売されている。しかしこれらの装置は薬剤との相互作用により保存中に皮膚に対する装置の付着性が低下してしまうことがある。このような接着性の低下は貼付剤にとって致命的な問題となりうる。

【０００３】また、薬剤の放出面部と皮膚への接着に関わる感圧性接着剤層とが分離された経皮治療用装置もいくつか提案されている。例えば特開昭６１－２６５１５０号公報には薬剤貯蔵槽とその外周に存在する接着剤の間を円周方向シールによって分離させた実施例が開示されている。実開昭６０－６３３４４号公報、実開昭６２－１８２９４２号公報、特開昭６２－１９５３２６号公報、特開平１－２２４３１２号公報、特公平４－４６５９２号公報、特表平６－５０３２５２号公報、特開平２－１２８３号公報及び特開昭６２－２１２３２０号公報などの実施例に示された経皮治療用装置も薬剤放出面周囲の感圧性接着剤層と薬剤貯蔵槽の相互作用を断ち切っている点では特開昭６１－２６５１５０号公報と共通している。しかし、これらの実施例にみられるような感圧性接着剤層を薬剤放出面の周囲に配置すると装置全体がかさばり皮膚への付着性が低下する。そこで付着性を上げるために感圧性接着剤層の面積を大きくする、もしくは接着力を上げることになり皮膚刺激の増加が懸念される。

【０００４】一方、薬物に関して言うと卵胞ホルモンに含まれるエストラジオールは、女性の生殖可能な時期に卵巣より分泌されるものである。従って、閉経前後の女性は主としてエストラジオールの欠乏を来たし、更年期障害や月経異常等の症状が生じる。現在これらの症状を改善する目的で経口剤投与等による治療法が行われているものの、胃腸等の消化管や肝臓等により迅速に代謝され不活化されるため、充分な薬効発現を期待するためには高用量のエストラジオールを服用しなければならない。また高用量のため副作用等の発現性が高まる恐れがある。そこで、経皮投与でエストラジオールの代謝を少なくし血中に到達させ治療に供しようとする試みがなされている。例えば、特公平６－５１６２３号公報及び特表平３－５０１３８６号公報ではエストラジオール等ホルモンをエタノールのゲル中に封入させ、コントロール膜により放出制御させているリザーバ型製剤に関して提案されている。しかし、これらはエタノールによる皮膚

刺激が頻発し、薬液との相互作用により粘着剤の凝集力が低下するという問題がある。一方、他のホルモンである黄体ホルモンを経皮より吸収させエストラジオール投与における副作用を抑える検討もなされている。例えば、特表平２－５００７４０号公報では、シリコーン系ポリマー基剤中にエストロゲンとプロゲストゲンを含有する経皮吸収製剤が提案され、特開平３－２２０１２１号公報にはアクリル酸エステル系ポリマー基剤中にエストロゲンを含有するゲル製剤が提案されている。しかし、これらの製剤では１７－β－エストラジオール、ノルエチステロン等を用いた時に徐放性が十分でないといった欠点を有していた。また、特開平４－３４２５３２号公報にはエストラジオールと黄体ホルモンを薬効成分とし、粘着剤として２－エチルヘキシルアクリレートとＮ－ビニル－２－ピロリドンからなるアクリル系粘着剤を主成分とする経皮吸収製剤が提案されている。しかし、アクリル系粘着剤は薬物放出性が低く、皮膚に対する刺激も強く長期連続投与に耐え難いものである。また、これら放出を制御されていない製剤は初期放出の急激な立ち上がりにより血中濃度が一時に上昇し副作用の発現が高まる恐れがある。

【０００５】

【発明が解決しようとする課題】本発明が解決しようとする課題は装置の保存中に薬剤との相互作用による付着性の低下及び感圧性接着剤層を周囲に配置することによるかさばりに伴う皮膚刺激の増加をなくすことである。また、本発明は治療に有効な量の薬物が薬剤液の貯蔵槽から薬剤放出層を通過して皮膚表面へと供給される装置に関するものであるが、装置の保存中においては薬剤放出面が密封されており装置の使用に際してこの密封性を解除し、保存中の薬剤損失を実質的になくすと共に、使用に際しては予定量の薬剤を正確かつ確実に患者に適用できる経皮治療用装置を提供しようとするものである。

【０００６】

【課題を解決するための手段】本発明者らは上記課題を解決するために鋭意研究を重ねた結果、経皮治療用装置において薬物の放出をコントロールし得る感圧性接着剤層からなる薬剤放出層を使用することにより薬剤の放出をコントロールしつつ、且つ漏出を防止できることを見出した。すなわち、薬物の放出をコントロールし得る感圧性接着剤層からなる薬剤放出層を有する本発明の経皮治療用装置により、良好な付着性が得られ、かさばりによる皮膚刺激の増加を防止できるとともに、保存中には薬剤の漏出を防止し、本装置を患者皮膚へ貼付した後においては治療に有効な量の薬剤が正確かつ確実に本装置より放出されることが可能となる。したがって、本発明は、

１）シンプルな構造による薬剤の放出コントロール、

２）薬剤の保存安定性の向上、

３）皮膚刺激性の低減、

４）皮膚への良好な付着性、

５）感圧性接着剤の高い凝集力、

を図った経皮治療用装置を提供することにある。

【０００７】本発明は、

（Ａ）　薬剤非透過性の裏打ち材層

（Ｂ）　裏打ち材層と薬剤放出層との間に、治療に有効な量の薬物が含有された薬剤貯蔵層、

（Ｃ）　薬物の放出をコントロールし得る感圧性接着剤層からなる薬剤放出層、よりなる少なくとも３個の層を有する経皮治療用装置に関する。本発明の経皮治療用装置は、前記した薬剤放出層の外側に、装置の使用に際して剥離することが可能な剥離ライナー層を有することもできる。また、本発明の薬剤の放出をコントロールする薬剤放出層は、感圧性接着剤層のほかに薬剤透過性フィルム（以下、多孔質層ともいう。）を包含することもできる。より詳細には、本発明は、ゴムエラストマー、粘着付与樹脂及び軟化剤を含有する感圧性接着剤、又は、これらの成分に更にアクリル系粘着剤を含有させてなる感圧性接着剤からなる薬物の放出をコントロールし得る感圧性接着剤層を含有する薬剤放出層を有する経皮治療用装置を提供することにある。さらに詳細には、本発明の感圧性接着剤層は、前記した感圧性接着剤を薬剤放出層の全面に塗布したものである。

【０００８】以下本発明を具体的に説明する。本発明の経皮治療用装置のひとつの形態として図１に示される層構造を有するものを挙げることができる。図１のものは、治療に有効な量の薬効成分を含有する液状の薬剤が裏打ち材層①と薬剤透過性フィルムの多孔質材③との間の薬剤貯蔵層②の中に封入されている。多孔質材③の外層には感圧性接着剤層④が積層され、薬剤を密封しておくための剥離ライナー⑤が被覆される。この剥離ライナー⑤は本装置の使用に際しては剥離除去されるものである。図２は、図１に示した本発明の経皮治療用装置の剥離ライナー⑤を除去した装置の状態を皮膚側から見た図である。また、ブレス層⑥は薬剤貯蔵層②の密封のために薬物透過フィルムと裏打ち材のシールを施した部分で有効放出面の外周に沿って深めにブレスされている。感圧性接着剤層④により剥離ライナー⑤との間に薬剤が貯留しないので剥離ライナー⑤の除去に伴う薬剤損失がなくなる。本装置を患者皮膚へ適用した時に薬剤放出層から薬剤が放出されることが可能となる。

【０００９】有効成分となる薬物は、生理的に活性な物質で経皮吸収性を有する必要があるものであれば特に制限はない。また、本発明の薬物は経皮吸収された後に生理活性を示すような、いわゆるプロドラッグであってもよい。例えば有効成分としては、卵胞ホルモンとして、エストラジオール、ジプロピオン酸エストラジオール、結合型エストロゲン、メストラノール、エストリオール、エキリン、エキレニンまたはそれらの誘導体として、安息香酸エストラジオール、エチニルエストラジオ

ール、吉草酸エストラジオール及びプロピオン酸エストリオール、トリプロピオン酸エストリオール、安息香酸酢酸エストリオール等が挙げられるが、本発明においては特にエストラジオールが用いられる。また、黄体ホルモンとしては、プロゲステロン、カプロン酸ヒドロキシプロゲステロン、酢酸メドロキシプロゲステロン、ジドロゲステロン、酢酸クロルマジノン、エチステロン、ジメチステロン、ノルエチステロン、酢酸ノルエチステロン、エナント酸ノルエチステロン、酢酸エチノジオール、酢酸メゲストロールまたはアリルエストレノール等が挙げられるが、本発明においては特に酢酸ノルエチステロンが好ましい。

【００１０】その他に本経皮治療用装置に有効な薬物としては、例えば、冠血管拡張剤（例：ニトログリセリン、硝酸イソソルビド、塩酸ジルチアゼム、ニフェジピン、ニコランジル、ニトレンジピン等）、局所麻酔剤（例：リドカイン、ベンゾカイン、塩酸プロカイン、テトラカイン等）、骨格筋弛緩剤（例：エペリゾン、チザニジン、トルペリゾン、イナペリゾン、ブリジノール、ダントロレン等）、抗高血圧症剤（例：クロニジン、レセルピン、硫酸グアネチジン、エホニジピン、ビンドロール、マロン酸ボピンドロール、カプトプリル、デラプリル等）、鎮痛剤（例：モルヒネ、塩酸ブプレノルフィン、クエン酸フェンタニル、ペンタゾシン、臭化水素酸エプタゾシン等）、排尿障害治療剤（例：塩酸クレンブテロール、酢酸オサテロン、塩酸チロリジン、塩酸オキシブチニン、フラボキサート等）、抗てんかん剤（例：ニトラゼパム、メプロバメート等）、抗パーキンソン病剤（例：クロルゾキサゾン、レボドパ等）、抗アレルギー剤（例：トラニラスト、アゼラスチン、ケトチフェン、メキタジン、イブジラスト、オキサトミド、エメダスチン等）、中枢神経作用薬（例：クロルプロマジン、ニトラゼパム、ジアゼパム、レセルピン、イミプラミン等）、消炎鎮痛剤（例：インドメタシン、ケトプロフェン、ジクロフェナク、ケトロラク、フェルビナク、フルルビプロフェン、ロキソプロフェン、テニダップ、エトドラグ、インドメタシンファルネシル等）、禁煙補助剤（例：ニコチン）、制吐剤（例：ハロペリドール、チミペロン、ベンペリドール、フロロバミド、ファニゾン等）、プロスタグランジン（例：PGE_1、$PGF_2\alpha$、PGE_2、PGI_2等）、抗めまい剤（例：ジフェニドール、ベタヒスチン等）、交感神経刺激剤（例：硫酸サルブタモール、塩酸ツロブテロール、塩酸プロカテロール、塩酸マブテロール等）、免疫調節剤（例：ＬＰＳ類、オーラノフィン、ロベンザリット等）、ポリペプチド系のホルモン剤（ＬＨ－ＲＨ、ＴＲＨ等）、抗エストロゲン剤（例：タモキシフェン、塩酸ファドロゾール等）、他のホルモン剤（例：テストステロン等）、などの種類の薬物が使用でき、配合目的によって異なるが治療に有効な量として通常薬剤に対して０．１～１０重量%の配合量が好ましく用いられる。また、これらの薬物は相互作用による不都合が生じない場合には必要に応じて２種類以上の併用も可能である。

【００１１】本発明の前記した薬物は、他の成分を添加して液状の薬剤として、薬剤貯蔵層に貯蔵させるのが好ましい。本発明の経皮治療用装置の液状の薬剤とするための基剤の組成としては、水成分の配合割合が２０～７０重量%、低級アルコールの配合割合は１０～４０重量%範囲が好ましい。吸収促進剤である脂肪アルコールの配合割合は０．１～１０重量%の範囲内が好ましい。保湿剤のグリセリンまたはポリエチレングリコールの配合割合は２０～４０重量%の範囲が好ましい。最後に刺激低減剤のグリセリンモノオレートまたはグリセリンモノラウレートもしくはそれらの混合物の配合割合は１～１０重量%の範囲が好ましいものであり、これらの各基剤は各々の配合割合の範囲でもって適宜処方される。また、これらは必要に応じてゲル化剤を加えられる。

【００１２】ゲル化剤としてはカルボキシビニル重合体、ポリアクリル酸ソーダ、ポリビニルピロリドン、ヒドロキシプロピルメチルセルロース、ヒドロキシエチルセルロース、ヒドロキシプロピルセルロース、メチルセルロース、カルボキシメチルセルロース等の適宜なゲル化剤が例示される。さらに必要に応じて紫外線吸収剤、抗酸化剤、防腐剤等の添加剤を加えてもよい。例えば紫外線吸収剤としては公知のＰ－アミノ安息香酸誘導体、アントラニル酸誘導体、サリチル酸誘導体、クマリン誘導体、アミノ酸誘導体、ベンゾトリアゾール誘導体、テトラゾール誘導体、イミダゾリン誘導体、ピリミジン誘導体、ジオキサン誘導体、フラン誘導体、ピロン誘導体、カンファー誘導体、核酸誘導体、アラントイン誘導体、ニコチン酸誘導体、シコニンあるいはビタミン６誘導体等が例示され、特に２－ヒドロキシ－４－メトキシベンゾフェノン誘導体などのベンゾフェノン誘導体が好適に用いられる。抗酸化剤としては例えばアスコルビン酸、ステアリン酸エステル、アスコルビン酸ナトリウム、トコフェロール（α－トコフェロール、β－トコフェロール、γ－トコフェロール、δ－トコフェロール等のｄ体、ｌ体、ｄｌ体）及びこれらのエステル誘導体、ノルジヒドログアセレチン酸、ジブチルヒドロキシトルエン、ブチルヒドロキシアニソール、ｔｅｒｔ－ブチルヒドロキシノン、没食子酸エステル（エチル、プロピル、イソアミル等のエステル）、１－オキソ－３－メチル－４－イソプロピルベンゼン等の適宜な抗酸化剤が例示される。

【００１３】次に、裏打ち材層について述べる。裏打ち材層となるフィルムは薬剤の漏出・揮散の防止のためにいわゆるバリア性に優れ、薬剤放出材層の多孔質材と容易に接着できるなどの性質を有する必要がある。また、装置を皮膚に貼付した際の適度な柔軟性があることが好ましい。裏打ち材フィルムの素材としては、上記の条件

を備えていれば特に限定はされないが、具体的にはアルミニウム、エチレンビニルアセテート共重合体またはそのケン化物、酢酸セルロース、セルロース、ナイロン、ポリエステル、ポリエチレン、ポリ塩化ビニリデン、ポリカーボネート、ポリビニルアルコール、ポリプロピレンなどが例としてあげられる。これらの素材は、フィルム状にするか、または必要に応じて紙・布状にしたものをフィルムと積層したり積層フィルム状に加工し、あるいは、アルミニウム蒸着、セラミック蒸着などの処理を行い、バリア性、薬剤放出材層との接着性等を改良することができる。

【００１４】ここで、本発明に使用できる好ましい薬剤の組成の一例を示す。本発明で使用される吸収促進剤としては炭素数７～２０までの脂肪酸、脂肪アルコールまたは脂肪酸エステルが好ましく特にラウリルアルコール及びミリスチルアルコールが特に高い吸収促進性を示しかつ比較的皮膚にたいして刺激性が少ない。また、保湿剤としてはソルビトール、ポリエチレングリコール、ジグリセリン、プロピレングリコール、ブチレングリコール、ジプロピレングリコール、ソディウムピロリドンカルボキシレート、エチルカルビトール、Ｄ－キシリトール、グリセリン、ヒアルロン酸が好ましくその中で特にグリセリンまたはポリエチレングリコールが好ましい。水成分については緩衝液が好ましく、特に広域緩衝液であるマックルベイン緩衝液が好ましい。刺激低減剤としては脂肪酸エステルまたはソルビトール脂肪酸エステルもしくはその混合物が好ましい。低級アルコールとしては特にエタノールまたはイソプロパノールが好ましい。

【００１５】薬剤透過性フィルムを形成する素材としては多孔質材であり、具体的には例えばエチレンビニルアセテート共重合体、セルロース、セルロースアセテート、ポリエステル、ポリエチレン、ポリプロピレン等があげられる。薬剤透過性フィルムは通気性を有する微多孔性フィルム状、紙状、布状、又は、スポンジ状の高分子の１種又は２種以上からなることができる。多孔質材についてはガーレー式通気度が１０～５００ｓｅｃ／１００ｃｃの範囲であることが好ましい。

【００１６】薬物の放出をコントロールし得る感圧性接着剤層は、装置を皮膚に付着させるための十分な接着力を有することが必要な条件である。また、皮膚に対する安全性に優れることが好ましい。本発明の感圧性接着剤層としては、ゴムエラストマー、粘着付与樹脂及び軟化剤を含有する感圧性接着剤、又は、これらの成分に更にアクリル系粘着剤を含有させてなる感圧性接着剤を用いたものが好ましい。本発明の感圧性接着剤層は、前記した感圧性接着剤を薬剤放出層の全面に塗布したものがより好ましい。

【００１７】具体的には、感圧性接着剤の成分として用いられるゴムエラストマーとしては、例えば、ポリイソブチレン（例えば、エクソン化学製の商品名：ビスタネックス、バスフ社製の商品名：オパノールとして入手可能なポリイソブチレンなど）、（Ａ－Ｂ）ｎ－Ａ型弾性重合体（例えば、シェル化学製のスチレン－ブタジエン－スチレンブロック共重合体（商品名：カリフレックスＴＲ－１１０１）、スチレン－イソプレン－スチレンブロック共重合体（商品名：カリフレックスＴＲ－１１０７、カリフレックスＴＲ－１１１１）、日本合成ゴム社製のスチレン－イソプレン－スチレンブロック共重合体（商品名：ＪＳＲ５０００，ＪＳＲ５１００）、日本ゼオン社製のスチレン－イソプレン－スチレンブロック共重合体（商品名：クインタック３４２１）等）などが挙げられる。これらゴムエラストマーは単独あるいは組合せて用いることができるが、ポリイソブチレンとスチレン－イソプレン－スチレンブロック共重合体との組合せが好ましい。ゴムエラストマーの感圧性接着剤中への配合量は５～５０重量%であり、好ましくは１０～４０重量%であり、さらに好ましくは１０～３０重量%である。

【００１８】感圧性接着剤の成分の粘着付与樹脂としては、脂環族飽和炭化水素樹脂（例えばアルコンＰ－１００（商品名））、ロジンエステル（例えばＫＥ－３１１、ＫＥ－１００（商品名）、スーパーエステルＳ－１００（商品名））、水添石油系樹脂（例えばフォーラル１０５（商品名））、テルペン系水素添加樹脂（例えばクリアロンＰ－１０５（商品名））等の粘着付与樹脂が例示される。感圧性接着剤中への配合量は５～５０重量%であり、好ましくは５～４０重量%であり、さらに好ましくは１０～３５重量%である。感圧性接着剤の成分の軟化剤としては、流動パラフィン、ポリブテン、ヒマシ油、綿実油、パーム油、ヤシ油、プロセスオイル等の軟化剤が例示される。感圧性接着剤中への配合量は１０～７０重量%であり、好ましくは１５～６０重量%であり、さらに好ましくは２０～５０重量%である。

【００１９】また、ゴムエラストマーとともに感圧性接着剤の成分として併用することもできるアクリル系粘着剤としては、特に、アルキル基の炭素数４～１８の（メタ）アクリル酸アルキルエステル単独重合体、または共重合体、あるいは、上記（メタ）アクリル酸アルキルエステルとその他の官能性モノマーとの共重合体が好適に用いられる。上記（メタ）アクリル酸エステルとしては、アクリル酸ブチル、アクリル酸イソブチル、アクリル酸ヘキシル、アクリル酸オクチル、アクリル酸－２－エチルヘキシル、アクリル酸イソオクチル、アクリル酸デシル、アクリル酸イソデシル、アクリル酸ラウリル、アクリル酸ステアリル、メタクリル酸メチル、メタクリル酸エチル、メタクリル酸ブチル、メタクリル酸イソブチル、メタクリル酸－２－エチルヘキシル、メタクリル酸イソオクチル、メタクリル酸デシル、メタクリル酸イソデシル、メタクリル酸ラウリル、メタクリル酸ステアリルなどが例示される。上記官能性モノマーの例として

は、水酸基を有するモノマー、カルボキシル基を有するモノマー、アミド基を有するモノマー、アミノ基を有するモノマー、ピロリドン環を有するモノマーなどが挙げられる。水酸基を有するモノマーとしては、２－ヒドロキシエチル（メタ）アクリレート、ヒドロキシプロピル（メタ）アクリレートなどのヒドロキシアルキル（メタ）アクリレートなどが例示される。カルボキシル基を有するモノマーとしては、アクリル酸、メタクリル酸などのα、β－不飽和カルボン酸：マレイン酸ブチルなどのマレイン酸モノアルキルエステル：マレイン酸：フマル酸：クロトン酸などが例示される。無水マレイン酸もマレイン酸と同様の共重合成分を与える。

【００２０】アミド基を有するモノマーとしては、アクリルアミド、ジメチルアクリルアミド、ジエチルアクリルアミドなどのアルキル（メタ）アクリルアミド：Ｎ－ブトキシメチルアクリルアミド、Ｎ－エトキシメチルアクリルアミドなどのＮ－アルコキシメチル（メタ）アクリルアミド、ジアセトンアクリルアミドなどが例示される。アミノ基を有するモノマーとしては、ジメチルアミノエチルアクリレートなどが例示される。ピロリドン環を有するモノマーとしてＮ－ビニル－２－ピロリドンなどが例示される。これらのアクリル系粘着剤の感圧性接着剤層中への配合量は０～８０重量％であり（ゴムエラストマー単独配合の場合は０重量％を意味する）、好ましくは５～６０重量％でありさらに好ましくは１０～３０重量％である。

【００２１】感圧性接着剤層の好適な膜厚は３０～３００μｍであり、３０μｍより薄いと付着性に問題が生じるし、３００μｍより厚ければ放出コントロールが困難になることがある。

【００２２】これらエラストマー、粘着付与樹脂、軟化剤及び／又はアクリル系粘着剤の組合せにより本願発明の皮膚安全性と放出コントロールを具備した経皮治療用装置となるのである。

【００２３】さらに本発明の感圧性接着剤層には、接着性・安全性・安定性の調製のために必要に応じて周知の添加剤を配合することができる。具体的にはスミカゲルＳＰ－５２０（商品名）、アクアキープ４ＳＨ（商品名）、アラソープ８００Ｆ（商品名）、サンウェット１Ｍ－１０００ＭＰＳ（商品名）等の吸水性高分子、酸化亜鉛、炭酸カルシウム、二酸化チタン、シリカ類等の無機充填剤、ポリエチレングリコール、クロタミトン等の溶解剤等の配合が適宜適量含有される。

【００２４】剥離ライナー層となるフィルムについては装置の保存中においては薬剤放出層からの薬剤揮散等を阻止できることが必要であり、また、この剥離ライナー層は装置の使用の際に剥離除去可能でなければならない。剥離ライナーフィルムの素材は具体的にはアルミニウム、セルロース、ポリエステル、ポリエチレン、ポリプロピレン等が使用可能であり必要に応じてこれらのフィルムを積層してもよい。また、その表面をシリコンあるいはフルオロカーボン等で処理するかまたはライナー素材中に周知の添加剤を配合するなどして剥離性を調整したりバリア性を調整してもよい。剥離ライナーには剥離する際のハンドリングが容易となるよう剥離のためのつまみ部をもうけることができる。薬剤放出層とこれを被覆する剥離ライナーとの間の接着性については装置の保存中においては密封接着されている必要があるが装置の使用に際してはかかる剥離ライナーを剥離除去できなければならない。したがって薬剤放出層とこれを被覆するライナーとの間の接着力は、裏打ち材層と薬剤放出層の接着力よりも低くなければならない。

【００２５】装置の形状は特に限定しないが例えば円形、楕円形、多角形等があげられる。装置の面積は１ｃｍ^2～２００ｃｍ^{2}の範囲にあることが好ましい。面積が１ｃｍ^{2}より狭いと剥離ライナーを剥がして装置を皮膚に貼ることが困難になり、また、２００ｃｍ^{2}より広くなると装置の装着感が悪くなる。一方装置の厚さについては薬剤貯蔵槽部における剥離ライナーをも含む装置の全厚さにおいて０．１～１５ｍｍの範囲であることが好ましい。厚さが０．１ｍｍより薄い場合薬剤放出面積あたりの投与薬剤量が少なくなることを余儀なくされ薬剤放出の持続性が短くなるので好ましくない。厚さが１５ｍｍより厚い場合患者の不意の動作により装置が剥離されてしまう可能性が高くなり好ましくない。

【００２６】このようにして得られた本経皮治療用装置は薬剤が裏打ち材層と薬剤放出層との間に封入された構造となっているので薬剤の性状として粘性の低い液状のものから粘性の高い液状のものまで幅広く許容することができテープ剤等と比較して薬剤組成の自由度が高いので安全性、安定性、有効性を好適に設計する上でのメリットは大きい。

【００２７】本発明の経皮吸収製剤の製造方法としては、特に制限はなく、通常の方法で製造することができる。例えば、本発明の薬剤放出層の調整方法としては感圧性接着剤層のすべての成分をヘキサン、トルエン、酢酸エチル等の有機溶媒に溶解させた後、剥離ライナーに展膏し有機溶剤を除去する。剥離ライナー側とは逆の感圧性接着剤層を多孔質材で覆い薬剤放出層を作成し、その薬剤放出層を所望の形状に切断し、別に調整した薬剤を多孔質材側に滴下し裏打ち材層とヒートシール後、このヒートシールの外周に沿って裁断し本発明の経皮治療用装置を得る。また、本発明の経皮吸収製剤の貯蔵される薬剤については、低級アルコール、保湿剤、水、刺激低減剤、吸収促進剤及び薬物を適宜処方し乳化試験機（日光ケミカルＥＴ－３Ａ型）により調整することができる。

【００２８】

【実施例】以下、実施例、試験例を挙げて本発明をより詳細に説明する。なお、実施例、比較例、参考例中の数

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値はすべて重量%基準である。　＊　＊【００２９】実施例１

感圧性接着剤の組成

スチレン－イソプレン－スチレンブロック共重合体	１０．５０
アクリル系粘着剤（アクリル酸－２－エチルヘキシル／酢酸ビニル共重合体）	１０．００
流動パラフィン	４９．３０
粘着付与剤（脂環族飽和炭化水素樹脂）	２０．００
ポリイソブチレン	１０．００
ジブチルヒドロキシトルエン	０．２０

この処方で上記に例示した製造方法に従い作製し、多孔　10※た。
質材を積層し所望の大きさに切断して薬剤放出層とし　※　【００３０】

薬剤組成

エタノール	２４．００
緩衝液	４０．００
グリセリン	２５．００
ラウリルアルコール	０．５０
グリセリンモノオレート	３．００
ソルビタンモノラウレート	１．００
カルボキシメチルセルロースナトリウム	３．５０
エストラジオール	１．００
酢酸ノルエチステロン	２．００

薬剤０．５ｇを多孔質材側に滴下し裏打ち材層とヒート　★明の経皮治療用装置を得た。
シールし、このヒートシールの外周に沿って裁断し本発★　【００３１】実施例２

感圧性接着剤の組成

スチレン－イソプレン－スチレンブロック共重合体	３０．００
アクリル系粘着剤（アクリル酸－２－エチルヘキシル／アクリル酸エチル・酢酸ビニル共重合体）	５．００
流動パラフィン	３０．５０
粘着付与剤（脂環族飽和炭化水素樹脂）	２５．００
ポリイソブチレン	５．００
ポリエチレングリコール２００	４．００
ジブチルヒドロキシトルエン	０．５０

この処方で上記の製造方法に従い作製し、多孔質材を積　☆【００３２】
層し所望の大きさに切断して薬剤放出層とした。　☆

薬剤組成

エタノール	２４．００
緩衝液	４０．５０
ポリエチレングリコール３００	２５．００
ラウリルアルコール	０．５０
グリセリンモノオレート	３．００
ソルビタンモノラウレート	１．００
ヒドロキシプロピルメチルセルロース４０００	２．００
エストラジオール	１．００
プロゲステロン	３．００

薬剤０．５ｇを多孔質材側に滴下し裏打ち材層とヒート　◆明の経皮治療用装置を得た。
シールし、このヒートシールの外周に沿って裁断し本発◆　【００３３】実施例３

感圧性接着剤の組成

スチレン－イソプレン－スチレンブロック共重合体	１５．００
アクリル系粘着剤（アクリル酸－２－エチルヘキシル／ビニルピロリドン共重合体）	１１．５０

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流動パラフィン	１４．５０
粘着付与剤（ロジンエステル）	３５．００
ポリイソブチレン	１５．００
クロタミトン	５．００
サンウェット１Ｍ－１０００ＭＰＳ	３．００
ジブチルヒドロキシトルエン	１．００

この処方で上記の製造方法に従い作製し、多孔質材を積　＊【００３４】
層し所望の大きさに切断して薬剤放出層とした。　＊

薬剤組成

エタノール	２４．００
緩衝液	４０．５０
ポリエチレングリコール４００	２５．００
ラウリルアルコール	０．５０
グリセリンモノオレート	３．００
ソルビタンモノラウレート	１．００
ヒドロキシプロピルメチルセルロース４０００	２．００
エストラジオール	１．００
酢酸メドロキシプロゲステロン	３．００

薬剤０．５ｇを多孔質材側に滴下し裏打ち材層とヒート　※明の経皮治療用装置を得た。
シールし、このヒートシールの外周に沿って裁断し本発※20　【００３５】実施例４

感圧性接着剤の組成

スチレン－イソプレン－スチレンブロック共重合体	２０．００
アクリル系粘着剤（アクリル酸／アクリル酸オクチル共重合体）	２０．００
流動パラフィン	３４．５０
粘着付与剤（脂環族飽和炭化水素樹脂）	１７．００
ポリイソブチレン	８．００
ジブチルヒドロキシトルエン	０．５０

この処方で上記の製造方法に従い作製し、多孔質材を積　★【００３６】
層し所望の大きさに切断して薬剤放出層とした。　★30

薬剤組成

エタノール	２４．００
緩衝液	４０．００
ポリエチレングリコール３００	２６．００
ミリスチルアルコール	１．００
グリセリンモノオレート	２．００
ヒドロキシプロピルメチルセルロース４０００	２．００
エストラジオール	１．００
酢酸ノルエチステロン	４．００

薬剤０．５ｇを多孔質材側に滴下し裏打ち材層とヒート　40☆明の経皮治療用装置を得た。
シールし、このヒートシールの外周に沿って裁断し本発☆　【００３７】実施例５

感圧性接着剤の組成

スチレン－イソプレン－スチレンブロック共重合体	２５．００
流動パラフィン	４２．００
粘着付与剤（脂環族飽和炭化水素樹脂）	２０．００
ポリイソブチレン	８．００
ポリエチレングリコール２００	４．００
ジブチルヒドロキシトルエン	１．００

この処方で上記の製造方法に従い作製し、多孔質材を積　【００３８】
層し所望の大きさに切断して薬剤放出層とした。　50

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薬剤組成

エタノール	２５．００
緩衝液	４１．００
ポリエチレングリコール３００	２５．００
ミリスチルアルコール	１．００
ソルビタンモノラウレート	１．００
ヒドロキシプロピルメチルセルロース４０００	２．００
エストラジオール	１．００
プロゲステロン	４．００

薬剤０．５ｇを多孔質材側に滴下し裏打ち材層とヒート　10＊明の経皮治療用装置を得た。
シールし、このヒートシールの外周に沿って裁断し本発＊　【００３９】実施例６

感圧性接着剤の組成

スチレン－イソプレン－スチレンブロック共重合体	１２．００
アクリル系粘着剤（アクリル酸－２－エチルヘキシル／酢酸ビニル共重合体）	１５．００
流動パラフィン	１７．８０
粘着付与剤（ロジンエステル）	３３．００
ポリイソブチレン	１５．００
クロタミトン	５．００
サンウェット１Ｍ－１０００ＭＰＳ	１．００
ジブチルヒドロキシトルエン	１．２０

この処方で上記の製造方法に従い作製し、多孔質材を積　※【００４０】
層し所望の大きさに切断して薬剤放出層とした。　※

薬剤組成

イソプロパノール	４０．００
緩衝液	２０．００
ポリエチレングリコール４００	３０．００
ミリスチルアルコール	１．００
ソルビタンモノラウレート	２．００
ヒドロキシプロピルメチルセルロース４０００	２．００
エストラジオール	１．００
酢酸メドロキシプロゲステロン	４．００

薬剤０．５ｇを多孔質材側に滴下し裏打ち材層とヒート　★明の経皮治療用装置を得た。
シールし、このヒートシールの外周に沿って裁断し本発★　【００４１】実施例７

感圧性接着剤の組成

スチレン－イソプレン－スチレンブロック共重合体	１２．００
アクリル系粘着剤（アクリル酸－２－エチルヘキシル／アクリル酸メチル共重合体）	５．５０
流動パラフィン	２３．００
粘着付与剤（脂環族飽和炭化水素樹脂）	５０．００
ポリイソブチレン	８．００
ジブチルヒドロキシトルエン	１．５０

この処方で上記の製造方法に従い作製し、多孔質材を積　☆【００４２】
層し所望の大きさに切断して薬剤放出層とした。　☆

薬剤組成

エタノール	１０．００
緩衝液	６１．００
ポリエチレングリコール４００	２０．００
ラウリルアルコール	１．００
ソルビタンモノラウレート	２．００

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ヒドロキシプロピルメチルセルロース４０００	２．００
エストラジオール	１．００
ノルエチステロン	３．００

薬剤０．５ｇを多孔質材側に滴下し裏打ち材層とヒート　＊明の経皮治療用装置を得た。
シールし、このヒートシールの外周に沿って裁断し本発＊　【００４３】実施例８

感圧性接着剤の組成

スチレン－イソプレン－スチレンブロック共重合体	１０．００
アクリル系粘着剤（アクリル酸－２－エチルヘキシル／ビニルピロリドン共重合体）	３０．００
流動パラフィン	２９．００
粘着付与剤（脂環族飽和炭化水素樹脂）	２０．００
ポリイソブチレン	１０．００
ジブチルヒドロキシトルエン	１．００

この処方で上記の製造方法に従い作製し、多孔質材を積　※【００４４】
層し所望の大きさに切断して薬剤放出層とした。　※

薬剤組成

エタノール	２４．００
緩衝液	４０．００
グリセリン	２５．００
ラウリルアルコール	０．５０
グリセリンモノオレート	３．００
ソルビタンモノラウレート	１．００
カルボキシメチルセルロースナトリウム	３．５０
塩酸ツロブテロール	３．００

薬剤０．５ｇを多孔質材側に滴下し裏打ち材層とヒート　★明の経皮治療用装置を得た。
シールし、このヒートシールの外周に沿って裁断し本発★　【００４５】実施例９

感圧性接着剤の組成

スチレン－イソプレン－スチレンブロック共重合体	３０．００
アクリル系粘着剤（アクリル酸－２－エチルヘキシル／酢酸ビニル共重合体）	１０．００
流動パラフィン	２０．００
粘着付与剤（脂環族飽和炭化水素樹脂）	２９．５０
ポリイソブチレン	５．００
ポリエチレングリコール２００	５．００
ジブチルヒドロキシトルエン	０．５０

この処方で上記の製造方法に従い作製し、多孔質材を積　☆【００４６】
層し所望の大きさに切断して薬剤放出層とした。　☆

薬剤組成

エタノール	２４．００
緩衝液	４０．５０
ポリエチレングリコール３００	２５．００
ラウリルアルコール	０．５０
グリセリンモノオレート	３．００
ソルビタンモノラウレート	１．００
ヒドロキシプロピルメチルセルロース４０００	２．００
インドメタシン	４．００

薬剤０．５ｇを多孔質材側に滴下し裏打ち材層とヒート　◆明の経皮治療用装置を得た。
シールし、このヒートシールの外周に沿って裁断し本発◆　【００４７】実施例１０

感圧性接着剤の組成

スチレン－イソプレン－スチレンブロック共重合体	１５．００

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アクリル系粘着剤（アクリル酸／アクリル酸オクチル共重合体）	１５．００
流動パラフィン	１４．００
粘着付与剤（脂環族飽和炭化水素樹脂）	３５．００
ポリイソブチレン	１５．００
クロタミトン	３．００
サンウェット１Ｍ－１０００ＭＰＳ	２．００
ジブチルヒドロキシトルエン	１．００

この処方で上記の製造方法に従い作製し、多孔質材を積層し所望の大きさに切断して薬剤放出層とした。　＊【００４８】　＊10

薬剤組成

エタノール	２４．００
緩衝液	４０．５０
ポリエチレングリコール４００	２５．００
ラウリルアルコール	０．５０
グリセリンモノオレート	３．００
ソルビタンモノラウレート	１．００
ヒドロキシプロピルメチルセルロース４０００	２．００
エストラジオール	１．００
酢酸メドロキシプロゲステロン	３．００

薬剤０．５ｇを多孔質材側に滴下し裏打ち材層とヒートシールし、このヒートシールの外周に沿って裁断し本発明の経皮治療用装置を得た。※　【００４９】実施例１１　※

感圧性接着剤の組成

スチレン－イソプレン－スチレンブロック共重合体	２１．００
アクリル系粘着剤（アクリル酸－２－エチルヘキシル／酢酸ビニル共重合体）	２．００
流動パラフィン	３１．００
粘着付与剤（脂環族飽和炭化水素樹脂）	１６．００
ポリイソブチレン	２９．００
ジブチルヒドロキシトルエン	１．００

この処方で上記の製造方法に従い作製し、多孔質材を積層し所望の大きさに切断して薬剤放出層とした。　★【００５０】　★

薬剤組成

エタノール	２０．００
緩衝液	４０．００
ポリエチレングリコール３００	３０．００
ミリスチルアルコール	１．００
グリセリンモノオレート	２．００
ヒドロキシプロピルメチルセルロース４０００	２．００
塩酸オキシブチニン	５．００

薬剤０．５ｇを多孔質材側に滴下し裏打ち材層とヒートシールし、このヒートシールの外周に沿って裁断し本発明の経皮治療用装置を得た。☆　【００５１】実施例１２　☆

感圧性接着剤の組成

スチレン－イソプレン－スチレンブロック共重合体	１４．００
アクリル系粘着剤（アクリル酸－２－エチルヘキシル／ビニルピロリドン共重合体）	５．００
流動パラフィン	７０．００
粘着付与剤（脂環族飽和炭化水素樹脂）	１０．００
ジブチルヒドロキシトルエン	１．００

この処方で上記の製造方法に従い作製し、多孔質材を積層し所望の大きさに切断して薬剤放出層とした。　50

【００５２】

薬剤組成

エタノール	２４．００
緩衝液	４１．００
ポリエチレングリコール３００	２５．００
ミリスチルアルコール	２．００
ソルビタンモノラウレート	１．００
ヒドロキシプロピルメチルセルロース４０００	２．００
ケトプロフェン	５．００

薬剤０．５ｇを多孔質材側に滴下し裏打ち材層とヒート　10＊明の経皮治療用装置を得た。
シールし、このヒートシールの外周に沿って裁断し本発＊　　【００５３】実施例１３

感圧性接着剤の組成

スチレン－イソプレン－スチレンブロック共重合体	５．００
アクリル系粘着剤（アクリル酸－２－エチルヘキシル／アクリル酸メチル共重合体）	８０．００
流動パラフィン	１０．００
粘着付与剤（脂環族飽和炭化水素樹脂）	５．００

この処方で上記の製造方法に従い作製し、多孔質材を積　※【００５４】
層し所望の大きさに切断して薬剤放出層とした。　※

薬剤組成

イソプロパノール	４０．００
緩衝液	２０．００
ポリエチレングリコール４００	３０．００
ミリスチルアルコール	１．００
ソルビタンモノラウレート	２．００
ヒドロキシプロピルメチルセルロース４０００	２．００
テストステロン	５．００

薬剤０．５ｇを多孔質材側に滴下し裏打ち材層とヒート　★明の経皮治療用装置を得た。
シールし、このヒートシールの外周に沿って裁断し本発★　　【００５５】実施例１４

感圧性接着剤の組成

スチレン－イソプレン－スチレンブロック共重合体	２０．００
アクリル系粘着剤（アクリル酸－２－エチルヘキシル／酢酸ビニル共重合体）	１３．５０
流動パラフィン	２３．００
粘着付与剤（脂環族飽和炭化水素樹脂）	３４．００
ポリイソプチレン	８．００
ジブチルヒドロキシトルエン	１．５０

この処方で上記の製造方法に従い作製し、多孔質材を積　☆【００５６】
層し所望の大きさに切断して薬剤放出層とした。　☆

薬剤組成

エタノール	１０．００
緩衝液	６１．００
ポリエチレングリコール４００	２０．００
ラウリルアルコール	１．００
ソルビタンモノラウレート	２．００
ヒドロキシプロピルメチルセルロース４０００	２．００
ノルエチステロン	４．００

薬剤０．５ｇを多孔質材側に滴下し裏打ち材層とヒート
シールし、このヒートシールの外周に沿って裁断し本発明の経皮治療用装置を得た。

【００５７】参考例１の製造方法を示す。剥離処理の施されたフィルムにアクリル系粘着剤（ＴＳ－６２０）を
50 乾燥後の厚さが約５０μｍとなるように展着し有機溶剤

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を除去する。その粘着剤の上に５ｃｍ² 円形の上質紙を積層しさらにその上から多孔質材を積層する。その上質紙が積層された多孔質材の上に別に調整した薬剤０．５ｇを滴下し裏打ち材層とヒートシールする。このヒートシールが中心となるように２０ｃｍ² 円形に裁断し試験片とする。参考例２～４の製造方法を示す。全ての成分をヘキサン、トルエン、酢酸エチル等の有機溶媒に溶解＊させ支持体に展膏し有機溶剤を除去した後ライナーで覆い所望の形状に切断し試験片となすかあるいは剥離処理の施されたフィルムに展膏後有機溶剤を除去し適当な支持体に圧着転写し試験片とする。

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【００５８】参考例

参考例１

感圧性接着剤

アクリル系粘着剤（ＴＳ－６２０：日本カーバイト社製）

薬剤組成

エタノール	２４．００
緩衝液	４０．００
グリセリン	２５．００
ラウリルアルコール	０．５０
グリセリンモノオレート	３．００
ソルビタンモノラウレート	１．００
カルボキシメチルセルロースナトリウム	３．５０
塩酸ツロブテロール	３．００

※² 円形に裁断し塩酸ツロブテロール製剤とした。

【００５９】参考例２

アクリル系粘着剤	９７．００
（商品名　ＴＳ－６２０：日本カーバイト社製）	固形分
エストラジオール	０．５０
酢酸ノルエチステロン	２．５０

★合製剤とした。

【００６０】参考例３

スチレン－イソプレン－スチレンブロック共重合体	２５．００
ポリイソブチレン	５．００
流動パラフィン	４２．００
粘着付与剤（水添脂環族炭化水素）	２５．００
エストラジオール	０．５０
酢酸ノルエチステロン	２．５０

☆合製剤とした。

【００６１】参考例４

シリコーン粘着剤	９２．００
	固形分
（商品名　３５５Ｍｅｄｉｃａｌａｄｈｅｓｉｖｅ：ダウコーニング社製）	
クロタミトン	５．００
エストラジオール	０．５０
酢酸ノルエチステロン	２．５０

この処方で上記の製造方法に従い作製し、所望の大きさに切断してエストラジオールと酢酸ノルエチステロン混合製剤とした。

【００６２】比較例

比較例１

エストラダームＴＴＳ（チバガイギー社製）

【００６３】比較例２

ニトロダームＴＴＳ（チバガイギー社製）

【００６４】試験例

試験例１．付着性試験

実施例の試験片と参考例１及び２並びに比較例の試験片につき下記の手法により付着性試験及び皮膚刺激性試験を行った。２０人の被験者（健常人、男性）の上腕部に試験片を貼り７２時間貼付し評価を行った。その結果を表１、２に示す。付着性試験では、

脱　　落：０

３／４剥離：１

１／２剥離：２

１／４剥離：３

50　エッジ剥離：４

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剥離なし　：５

の５段階で評価し、被験者の平均を表１中にスコアーとして示した。表１中に示したスコアーからも明らかなように、比較例では７２時間の貼付において１／２剥離以上が半数以上に認められ（スコアー１．７）、参考例１では１／４剥離が半数以上認められた（スコアー３．４）のに対し実施例では剥離なしがほとんどであった（スコアー４．２～５．０）。また、皮膚刺激性試験については、

紅斑なし　：０

非常に軽度な紅斑　：１

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＊明らかな紅斑　：２

中程度ないし強い紅斑　：３

の４段階の評価を行い、被験者の平均を表２中にスコアーとして示した。表２中のスコアーからも明らかなように、参考例１、２及び比較例の半数以上が明らかな紅斑を認めた（スコアー１．７～２．８）のに対し実施例では非常に軽度な紅斑以下であった（スコアー０．０～０．３）。

【００６５】

【表１】

＊

被験者	実施例１	実施例２	実施例３	比較例１	比較例２	参考例１
A	5	4	5	1	1	4
B	5	3	5	0	1	3
C	5	4	5	2	1	3
D	5	5	5	1	3	4
E	5	5	5	3	2	4
F	5	4	5	2	1	3
G	5	4	5	1	2	3
H	5	5	4	2	2	3
I	5	4	5	2	2	3
J	5	4	5	3	2	4
ｽｺｱｰ	5.0	4.2	4.9	1.7	1.7	3.4

紅斑　：0
3/4剥離　：1
1/2剥離　：2
1/4剥離　：3
ｴｯｼﾞ剥離：4
剥離なし：5

【００６６】

【表２】

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	被験者	A	B	C	D	E	F	G	H	I	J	スコアー
剥離後30分	実施例 1	0	1	0	0	1	0	0	0	0	1	0.3
	実施例 2	0	1	0	1	0	0	1	0	0	0	0.3
	実施例 3	1	0	1	0	0	0	0	0	0	1	0.3
	比較例 1	2	3	2	3	3	2	3	2	2	3	2.5
	比較例 2	2	2	3	3	2	2	2	2	2	2	2.2
	参考例 1	3	3	3	2	3	2	3	3	3	3	2.8
	参考例 2	3	2	3	3	3	3	3	2	2	2	2.6
剥離後24時間	実施例 1	0	0	0	0	0	0	0	0	0	0	0.0
	実施例 2	0	0	0	0	0	0	0	0	0	0	0.0
	実施例 3	0	0	0	0	0	0	0	0	0	0	0.0
	比較例 1	2	2	2	3	3	2	2	2	2	2	2.2
	比較例 2	1	2	3	2	2	1	2	2	1	2	1.8
	参考例 1	2	2	1	1	2	2	2	1	2	2	1.7
	参考例 2	2	2	2	2	2	2	2	2	2	2	2.0

紅潤なし　　:0
非常に軽度な紅潤　:1
明らかな紅潤　　:2
中程度ないし強い紅潤:3

【００６７】試験例２．安定性試験
実施例及び参考例１の各試験片を５０°Ｃ・２ケ月保存し各試験片の重量変化及び薬剤の漏れについて確認した。重量変化が１０％以上あった試験片は×それ以外は○とした。薬剤漏れについてはライナーを除去する際にライナーへの薬剤の付着のあるものは×それ以外は○とした。結果は表３に示す。重量変化及び薬剤の漏れが参考例１では×であるのに対し実施例では全てが○であった。

【００６８】
【表３】

	実施例1	実施例2	実施例3	参考例1
重量変化	○	○	○	×
薬剤漏れ	○	○	○	×

【００６９】試験例３．凝集力試験
実施例及び比較例の試験片をそれぞれステンレス板に貼りしばらく放置した後ゆっくりと指で試験片を剥離しその剥離の際の状態観察を行った。ステンレス板に粘着剤残りのあるものは×残らないものは○さらに糸曳きのあるものは×ないものは○とし評価を行った。その結果を表４に示す。実施例では粘着剤残り及び糸曳きが全く認められなかったのに対し比較例では糸曳きが全てに認められた。

【００７０】
【表４】

	実施例1	実施例2	実施例3	比較例1	比較例2
粘着剤残り	○	○	○	×	×
糸曳き	○	○	○	×	×

【００７１】試験例４．放出試験
参考例及び実施例の試験片につき放出試験を回転シリンダー法により行った。試験条件としては試験液９００ｍｌ、試験液温度３２．０±０．５°Ｃ、シリンダー回転数５０ｒｐｍで行った。結果を図３，４に示す。参考例のものが立ち上がり急激に上昇し、後半落ちるのに対し、本発明の実施例のものは一定の放出量（制御された）のものであることがわかった。参考例の試験片が放

出制御されない一次放出となるのに対し、実施例のものは放出制御されたパターンを示し、本発明の経皮治療用装置が治療に有効な量の薬物を正確かつ確実に放出することが示された。

【００７２】

【発明の効果】本発明の経皮治療用装置により、装置の保存中に薬剤との相互作用による付着性の低下及び感圧性接着剤層を周囲に配置することによるかさばりに伴う皮膚刺激の増加をなくすことができる。また、本発明は治療に有効な量の薬物が薬剤液の貯蔵槽から薬剤放出層を通過して皮膚表面へと供給される装置であるから、装置の保存中においては薬剤放出面が密封されており装置の使用に際してこの密封性を解除し、保存中の薬剤損失を実質的になくすと共に、使用に際しては予定量の薬剤を正確かつ確実に患者に適用することができる。

【図面の簡単な説明】

＊【図１】本発明の経皮治療用装置のひとつの形態を図示したものである。

【図２】本発明の経皮治療用装置のひとつの形態の剥離ライナー⑤を除去した装置の状態を皮膚側から見た図である。

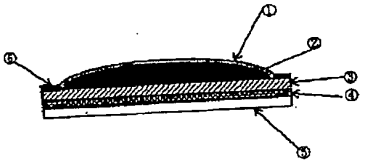
【図３】実施例および参考例の装置による卵胞ホルモン放出試験の結果を示したものである。

【図４】実施例および参考例の装置による黄体ホルモン放出試験の結果を示したものである。

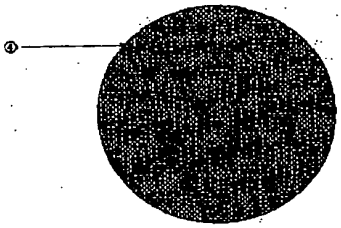
【符号の説明】

① 裏打ち材層
② 薬剤貯蔵層
③ 薬剤透過性フィルム（多孔質層）
④ 感圧性接着剤層
⑤ 剥離ライナー
＊ ⑥ ブレス層

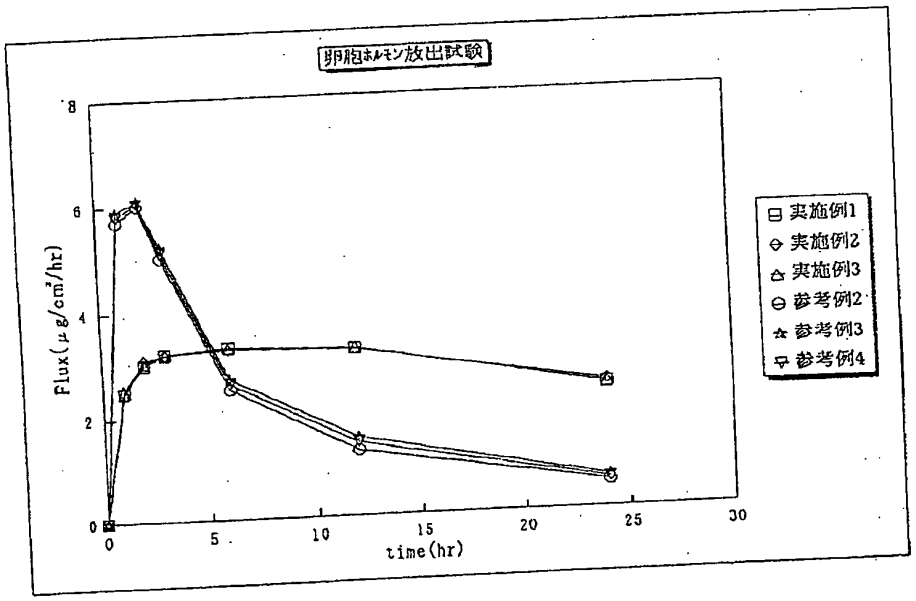
【図１】



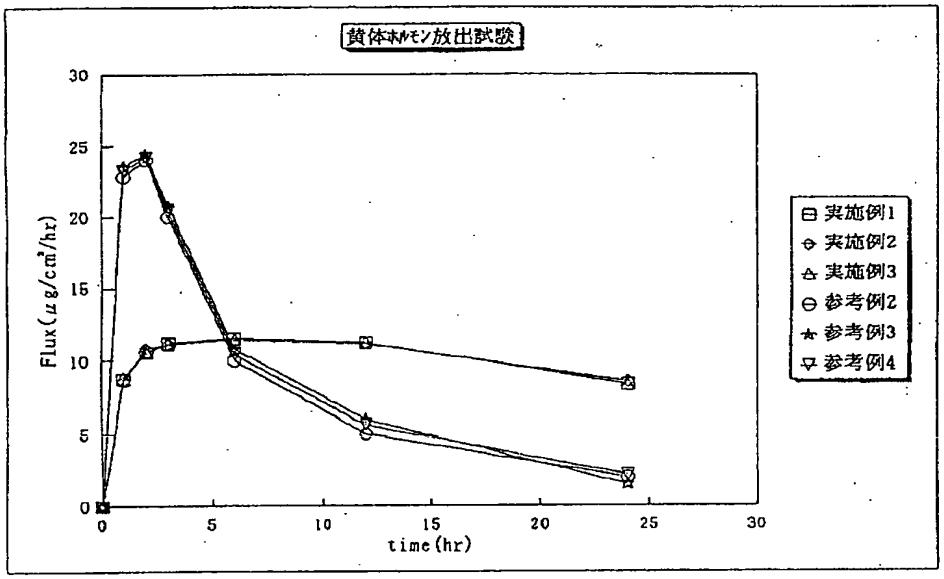
【図２】



【図３】



【図４】



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MAKI MASAYOSHI

(54) DEVICE FOR PERCUTANEOUS THERAPY

(57)Abstract:
PROBLEM TO BE SOLVED: To provide a device for a percutaneous therapy, capable of inhibiting the leakage of a liquid medicine from a medicine-storing layer during the storage of the device by laminating a medicine release-controlling pressure-sensitive adhesive to a medicinereleasing surface.
SOLUTION: This device for a percutaneous therapy has at least three layers of (A), (B) and (C). (A) A medicine-impermeable backing material layer. (B) A medicine-storing layer disposed between the backing material layer and a medicine-releasing layer and containing a medicine in an amount effective for the therapy. (C) A medicinereleasing layer comprising a pressure-sensitive adhesive layer capable of controlling the release of the medicine. The device can prevent the deterioration of adhesivity by the interaction of an adhesive with the medicine during the storage of the device, and the increase of a skin irritation accompanied by the increase in the volume of a device by disposing a pressure-sensitive adhesive on the periphery of the device. After the device is adhered to the skin of a patient, the medicine in an amount effective for the therapy of the patient can accurately and surely be released from the device.

LEGAL STATUS

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[Date of extinction of right]

* NOTICES *

1.This document has been translated by computer. So the translation may not reflect the original precisely.
2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

CLAIMS

[Claim(s)]
[Claim 1] (A) Backing material layer of drugs nontransparent nature (B) Drugs storage reservoir which the drug of an amount effective in a therapy contained between the backing material layer and the drugs emission layer (C) Equipment for an endermic therapy which has the drugs emission layer which consists of a pressure sensitive adhesive layer which can control emission of a drug, and at least three layers which become more.
[Claim 2] Equipment for an endermic therapy according to claim 1 which has the separator layer which can be exfoliated on the occasion of use of equipment on the outside of a drugs emission layer.
[Claim 3] Equipment for an endermic therapy according to claim 1 or 2 with which the drugs emission layer which controls emission of drugs consists of a drugs permeability film and a pressure sensitive adhesive layer.
[Claim 4] Equipment for an endermic therapy according to claim 1, 2, or 3 with which it comes to blend a pressure sensitive adhesive layer a softener and/or an acrylic binder with a rubber elastomer, a tackifier, and a list.
[Claim 5] Equipment for an endermic therapy according to claim 4 10 - 70 % of the weight and whose acrylic binder 5 - 50 % of the weight and a softener are [a pressure sensitive adhesive layer / a rubber elastomer] 0 - 80 % of the weight to pressure sensitive adhesive **** weight for 5 - 50 % of the weight, and a tackifier.
[Claim 6] Equipment for an endermic therapy given in any 1 term of claims 3-5 which a drugs permeability film becomes from one sort of the macromolecule of the shape of the shape of the shape of a fine porosity film which has permeability, and paper, blanket-like, or sponge, or two sorts or more.
[Claim 7] Equipment for an endermic therapy given in any 1 term of claims 1-6 whose drugs are estrogen and/or corpus luteal hormone.
[Claim 8] Equipment for an endermic therapy according to claim 7 which is one sort which estrogen becomes from estradiol, estrone, estriol, equilin, equilenins, or those derivatives, and corpus luteal hormone becomes from progesterone, caproic-acid PIDOROKISHI progesterone, medroxyprogesterone acetate, dydrogesterone, chlormadinone acetate, the ethisterone, the dimethisterone, norethisterone, acetic-acid norethisterone, enanthic acid norethisterone, acetic-acid ethynodiol, the megestrol acetate, allylestrenol, or those derivatives, or two sorts or more.
[Claim 9] Equipment for an endermic therapy given in any 1 term of claims 1-8 to which drugs come to contain lower alcohol, a moisturizer, water, a stimulus reduction agent, and absorption enhancers.
[Claim 10] Equipment for an endermic therapy according to claim 9 with which a moisturizer contains [a stimulus reduction agent] 20 to 70% of the weight 20 to 40% of the weight ten to 40% of the weight, and water comes for lower alcohol to contain [drugs] 0.1 - 10 % of the weight of absorption enhancers one to 10% of the weight.

[Translation done.]

DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Field of the Invention] This invention relates to the field of endermic medication. It is related with the equipment for an endermic therapy which is equipment for an endermic therapy which made it possible to control the exsorption from the drug storage tank of the liquefied drugs under preservation of equipment, and is characterized by the drugs of a quantum being certainly [correctly and] applicable to a patient beforehand by carrying out the laminating of the drugs emission control pressure sensitive adhesive to a detail more in a drug release side.

[0002]

[Description of the Prior Art] In the field of an endermic therapy, equipments for an endermic therapy, such as Estraderm (trade name) and nitro DAMU (trade name), are already developed and sold now. However, as for these equipments, the adhesion of the equipment to the skin may fall during preservation by the interaction with drugs. Such an adhesive fall can pose a problem fatal to patches.

[0003] Moreover, some equipments for an endermic therapy with which the emission surface part of drugs and the pressure sensitive adhesive layer in connection with adhesion on the skin were separated are also proposed. For example, the example which made between a drugs storage tank and the adhesives which exist in the periphery divide into JP,61-265150,A with a circumferencial direction seal is indicated. The equipment for an endermic therapy shown in examples, such as JP,60-63344,U, JP,62-182942,U, JP,62-195326,A, JP,1-224312,A, JP,4-46592,B, a ****** No. 503252 [six to] official report, JP,2-1283,A, and JP,62-212320,A, is also common in JP,61-265150,A in that the pressure sensitive adhesive layer of the perimeter of a drugs emission side and the interaction of a drugs storage tank are cut off. However, if a pressure sensitive adhesive layer which is seen by these examples is arranged around a

drugs emission side, the whole equipment will be bulky and the adhesion to the skin will fall. Then, in order to raise adhesion, or it enlarges area of a pressure sensitive adhesive layer, adhesive strength will be raised and we are anxious about the increment in a skin stimulus.

[0004] The estradiol contained in estrogen on the other hand when it says about a drug is secreted from the ovary at the stage when it can reproduce female. Therefore, the woman before and behind a menopause mainly causes lack of estradiol, and symptoms, such as menopausal disorders and an emmeniopathy, produce her. Although the cure by oral agent administration etc. is performed for the purpose which improves these symptoms now, since alimentary canals, liver, etc., such as the stomach and intestines, are metabolized quickly and inactivation is carried out, in order to expect sufficient drug effect manifestation, high-dose estradiol must be taken. Moreover, there is a possibility that manifestation nature, such as a side effect, may increase for a high dose. Then, the attempt with which is going to lessen the metabolic turnover of estradiol by dermal administration, and tends to be made to reach into blood, and it is going to present a therapy is made. For example, in JP,6-51623,B and a ****** No. 501386 [three to] official report, hormone, such as estradiol, is made to enclose into the gel of ethanol, and it is proposed about the reservoir mold pharmaceutical preparation which carries out emission control with the control film. However, the skin stimulus by ethanol occurs frequently and these have the problem that the cohesive force of a binder declines by the interaction with a drug solution. Examination which is made to absorb from transderma the corpus luteal hormone which is other hormone on the other hand, and suppresses the side effect in estradiol administration is also made. For example, in the ****** No. 500740 [two to] official report, estrogen and the percutaneous absorption pharmaceutical preparation containing the progestogen are proposed in a silicone system polymer basis, and the gel pharmaceutical preparation which contains estrogen in an acrylic ester system polymer basis is proposed by JP,3-220121,A. However, in these pharmaceutical preparation, when 17-beta-estradiol, norethisterone, etc. were used, it had the fault that sustained-release was not enough. Moreover, the percutaneous absorption pharmaceutical preparation which uses estradiol and corpus luteal hormone as a drug effect component at JP,4-342532,A, and uses as a principal component the acrylic binder which consists of 2-ethylhexyl acrylate and an N-vinyl-2-pyrrolidone as a binder is proposed. However, drug release nature is low, and the stimulus to the skin of an acrylic binder is strong, and it is intolerable to long-term repetitive administration. Moreover, the pharmaceutical preparation by which these emission is controlled has a possibility that blood drug concentration may rise at a

stretch by the rapid standup of initial emission, and the manifestation of a side effect may increase.

[0005]

[Problem(s) to be Solved by the Invention] The technical problem which this invention tends to solve is a thing which depend the adhesive fall and pressure sensitive adhesive layer by the interaction with drugs on arranging around during preservation of equipment and for which the increment in the skin stimulus in accordance with being bulky is abolished. Moreover, although this invention relates to the equipment with which the drug of an amount effective in a therapy passes a drugs emission layer from the storage tank of drugs liquid, and is supplied to a skin front face While the drugs emission side is sealed during preservation of equipment, canceling this sealing performance on the occasion of use of equipment and abolishing the drugs loss under preservation substantially, it is going to offer the equipment for an endermic therapy which can apply the drugs of a quantum to a patient correctly and certainly beforehand on the occasion of use.

[0006]

[Means for Solving the Problem] this invention persons found out that exsorption could be prevented, controlling emission of drugs by using the drugs emission layer which consists of a pressure sensitive adhesive layer which can control emission of a drug in the equipment for an endermic therapy as a result of repeating research wholeheartedly, in order to solve the above-mentioned technical problem. That is, while being able to prevent the increment in a skin stimulus which depends for acquiring good adhesion by the equipment for an endermic therapy of this invention which has the drugs emission layer which consists of a pressure sensitive adhesive layer which can control emission of a drug, and being bulky, exsorption of drugs prevents during preservation, and after sticking this equipment to the patient skin, it becomes that it is possible in the drugs of an amount effective in a therapy being emitted from this equipment correctly and certainly. therefore, this invention -- 1 -- it is in offering the equipment for an endermic therapy which planned emission control of the drugs by simple structure, improvement in the preservation stability of two drugs, reduction of 3 skin irritation, good adhesion to the 4 skin, and high cohesive force of five pressure sensitive adhesives.

[0007] This invention (A) Backing material layer of drugs nontransparent nature (B) Drugs storage reservoir which the drug of an amount effective in a therapy contained between the backing material layer and the drugs emission layer (C) It is related with the equipment for an endermic therapy which has the drugs emission layer which consists of a pressure sensitive adhesive layer which can control emission of a drug, and

at least three layers which become more. The equipment for an endermic therapy of this invention can also have the separator layer which can be exfoliated on the occasion of use of equipment on the outside of the above mentioned drugs emission layer. Moreover, the drugs emission layer which controls emission of the drugs of this invention can also include the drugs permeability film (henceforth a porous layer) other than a pressure sensitive adhesive layer. This invention is more at a detail to offer the equipment for an endermic therapy which has a drugs emission layer containing the pressure sensitive adhesive layer which can control emission of the drug which consists of a pressure sensitive adhesive containing a rubber elastomer, a tackifier, and a softener, or a pressure sensitive adhesive which makes it come further to contain an acrylic binder for these components. Furthermore, the pressure sensitive adhesive layer of this invention applies the above mentioned pressure sensitive adhesive to a detail all over a drugs emission layer.

[0008] This invention is explained concretely below. What has the layer structure shown in drawing 1 as one gestalt of the equipment for an endermic therapy of this invention can be mentioned. The liquefied drugs containing the drug effect component of an amount with the thing of drawing 1 effective in a therapy are enclosed in drugs storage reservoir ** between backing material layer ** and porosity material ** of a drugs permeability film. The laminating of the pressure sensitive adhesive layer ** is carried out to the outer layer of porosity material **, and separator ** for sealing drugs is covered. On the occasion of use of this equipment, exfoliation removal of this separator ** is carried out. Drawing 2 is drawing which looked at the condition of equipment of having removed separator ** of the equipment for an endermic therapy of this invention shown in drawing 1 , from the skin side. Moreover, press layer ** is pressed depth along with the periphery of an effective emission side in the part which gave the drug transparency film and the seal of backing material for seal of drugs storage reservoir **. Since drugs do not store between separator **s by pressure sensitive adhesive layer **, the drugs loss accompanying removal of separator ** is lost. When this equipment is applied to the patient skin, it becomes possible from a drugs emission layer to emit drugs.

[0009] If the drug used as an active principle needs to have percutaneous absorption by the activity matter physiologically, there will be especially no limit. Moreover, after percutaneous absorption of the drug of this invention is carried out, it may be the so-called prodrug as shows bioactive. For example, as an active principle, as estrogen, as estradiol, the estradiol dipropionate, estrogens conjugated, mestranol, estriol, equilin, equilenins, or those derivatives, although estradiol benzoate, ethinylestradiol, estradiol

valerate and estriol propionate, estriol tripropionate, estriol acetate benzoate, etc. are mentioned, estradiol is used especially in this invention. Moreover, as corpus luteal hormone, although progesterone, hydroxyprogesterone caproate, medroxyprogesterone acetate, dydrogesterone, chlormadinone acetate, the ethisterone, the dimethisterone, norethisterone, acetic-acid norethisterone, enanthic acid norethisterone, acetic-acid ethynodiol, the megestrol acetate, or allylestrenol is mentioned, especially in this invention, acetic-acid norethisterone is desirable.

[0010] in addition, as a drug effective in the equipment for this endermic therapy for example, a coronary vasodilator (example: -- nitroglycerin and isosorbide dinitrate --) Diltiazem hydrochloride, nifedipine, nicorandil, nitrendipine, etc., Local anesthetic (example: lidocaine, benzocaine, procaine hydrochloride, tetracaine, etc.), a skeletal muscle relaxant (INAPERIZON example: -- eperisone, teaser NIJIN, and tolperisone --) anti-hypertension agents (example: -- clonidine --), such as pridinol and a dantrolene Reserpine, guanethidine sulfate, EHONIJIPIN, pindolol, bopindolol malonate, painkillers (example: -- morphine and buprenorphine hydrochloride --), such as captopril and delapril Fentanyl citrate, pentazocine, eptazocine hydrobromide, etc., a dysuria therapy agent (hydrochloric acid CHIRORIJIN [and] example: -- clenbuterol hydrochloride --) [acetic acid] antiepiletic agents (example: -- nitrazepam --), such as oxybutynin hydrochloride and hula BOKISATO anti-Parkinson's disease agents (example: -- the chlorzoxazone --), such as meprobamate antiallergic agents (example: -- tranilast and azelastine --), such as REPODOPA Ketotifen, mequitazine, ibudilast, oxatomide, EMEDASUCHIN, etc., a central nervous system acting drug (example: -- chlorpromazine, nitrazepam, and diazepam --) antiphlogistic sedative drugs (example: -- indomethacin --), such as reserpine and imipramine Ketoprofen, diclofenac, ketorolac, felbinac, flurbiprofen, Loxoprofen, tenidap, ETODORAGU, indometacin farnesil, etc., smoking cessation aids (example: nicotine) and an antiemetic drug (example: -- haloperidol and timiperone --) prostagladins (example :P [1] GE and PGF2alpha --), such as benperidol, FURoROPAMIDO, and FANIZON PGE2, PGI2 grade, an anti-dizziness agent (example: diphenidol, betahistine, etc.), a sympathetic nerve stimulant (example: -- salbutamol sulfate, tulobuterol hydrochloride, and procaterol hydrochloride --) immunity modifiers (example: -- LPS and auranofin --), such as a hydrochloric-acid MAPUTE roll The hormone drug of polypeptide systems, such as lobenzarit, (LH-RH, TRH, etc.), The drug of the class of anti-estrogen agents (example: tomoxifen, a hydrochloric acid a fado ROZORU etc.), other hormone drugs (example: testosterone etc.), etc. can be used, and although it changes with combination purposes, 0.1 - 10% of the weight of loadings are usually preferably used to drugs as an amount

effective in a therapy. Moreover, when un-arranging according to an interaction does not arise, two or more kinds of concomitant use is also possible for these drugs if needed.

[0011] As for the drug which this invention described above, it is desirable to add other components and to make it store in a drugs storage reservoir as liquefied drugs. As a presentation of the basis for considering as the liquefied drugs of the equipment for an endermic therapy of this invention, the 10 - 40-% of the weight range has [the blending ratio of coal of lower alcohol] the desirable blending ratio of coal of a water component 20 to 70% of the weight. The blending ratio of coal of the fatty alcohol which is absorption enhancers has 0.1 - 10% of the weight of desirable within the limits. The glycerol of a moisturizer or the blending ratio of coal of a polyethylene glycol has 20 - 40% of the weight of the desirable range. Finally, the blending ratio of coal of the glycerol mono-olate of a stimulus reduction agent, glycerine monolaurate, or those mixture has 1 - 10% of the weight of the desirable range, and is suitably prescribed as each of these bases are also in the range of each blending ratio of coal. Moreover, these can add a gelling agent if needed.

[0012] As a gelling agent, proper gelling agents, such as a carboxy vinyl polymerization object, sodium polyacrylate, a polyvinyl pyrrolidone, hydroxypropyl methylcellulose, hydroxyethyl cellulose, hydroxypropylcellulose, methyl cellulose, and a carboxymethyl cellulose, are illustrated. Furthermore, additives, such as an ultraviolet ray absorbent, an anti-oxidant, and antiseptics, may be added if needed. For example, P-aminobenzoic-acid derivative well-known as an ultraviolet ray absorbent, an anthranilic-acid derivative, salicylic acid derivatives, a coumarin derivative, an amino acid derivative, a benzotriazol derivative, a tetrazole derivative, an imidazoline derivative, a pyrimidine derivative, a dioxane derivative, a furan derivative, a pyrone derivative, a camphor derivative, a nucleic-acid derivative, an allantoin derivative, a nicotinic-acid derivative, a shikonin, or vitamin 6 derivative is illustrated, and benzophenone derivatives, such as a 2-hydroxy-4-methoxybenzophenone derivative, are used especially suitably. As an anti-oxidant, proper anti-oxidants, such as an ascorbic acid, stearic acid ester, sodium ascorbate, tocopherols (d bodies, such as alpha-tocopherol, beta-tocopherol, gamma-tocopherol, and delta-tocopherol, l bodies, dl object) and these ester derivatives, the NORUJIHIDOROGUASE retinoic acid, dibutylhydroxytoluene, burylhydroxyanisole, tert-butyl BIDOROKISHINON, gallate (ester, such as ethyl, propyl, and isoamyl), and 1-oxo--3-methyl-4-isopropylbenzene, are illustrated.

[0013] Next, a backing material layer is described. The film used as a backing material layer needs to be excellent in the so-called barrier property for prevention of the

exsorption and vaporization of drugs, and needs to have the property of being able to paste up easily with the porosity material of a drugs emission material layer. Moreover, it is desirable that there is moderate flexibility at the time of sticking equipment on the skin. Although especially limitation will not be carried out as a material of a backing material film if it has the above-mentioned conditions, aluminum, an ethylene vinyl acetate copolymer or its saponification object, cellulose acetate, a cellulose, nylon, polyester, polyethylene, a polyvinylidene chloride, a polycarbonate, polyvinyl alcohol, polypropylene, etc. are specifically raised as an example. These materials can carry out the laminating of what made the shape of a film or was made paper and blanket-like if needed to a film, can process it in the shape of a laminated film, or can process the vacuum plating of aluminium, ceramic vacuum evaporationo, etc., and can improve barrier property, an adhesive property with a drugs emission material layer, etc.

[0014] Here, an example of a presentation of the desirable drugs which can be used for this invention is shown. As absorption enhancers used by this invention, the fatty acid, fatty alcohol, or fatty acid ester to carbon numbers 7-20 shows sorbefacient [with desirable especially especially expensive lauryl alcohol and myristyl alcohol], and the skin has stimulative [comparatively very little]. Moreover, as a moisturizer, a sorbitol, a polyethylene glycol, diglycerol, propylene glycol, a butylene glycol, dipropylene glycol, sodium pyrrolidone carboxylate, ethyl carbitol, D-xylitol, a glycerol, and hyaluronic acid are desirable, and a glycerol or a polyethylene glycol is desirable especially in it. About a water component, the buffer solution is desirable and the MAKKURU vein buffer solution which is especially the broader-based buffer solution is desirable. As a stimulus reduction agent, fatty acid ester, sorbitol fatty acid ester, or its mixture is desirable. Especially as lower alcohol, ethanol or isopropanol is desirable.

[0015] As a material which forms a drugs permeability film, it is porosity material, and an ethylene vinyl acetate copolymer, a cellulose, cellulose acetate, polyester, polyethylene, polypropylene, etc. are specifically raised. A drugs permeability film can consist of one sort of the macromolecule of the shape of the shape of the shape of a fine porosity film which has permeability, and paper, blanket-like, or sponge, or two sorts or more. About porosity material, it is desirable that it is the range whose gar rhe type permeability is 10-500sec / 100 cc.

[0016] The pressure sensitive adhesive layers which can control emission of a drug are conditions with required having sufficient adhesive strength for making equipment adhere to the skin. Moreover, excelling in the safety to the skin is desirable. As a pressure sensitive adhesive layer of this invention, the thing using the pressure sensitive adhesive containing a rubber elastomer, a tackifier, and a softener or the

pressure sensitive adhesive which makes these components come to contain an acrylic binder further is desirable. As for the pressure sensitive adhesive layer of this invention, what applied the above mentioned pressure sensitive adhesive all over the drugs emission layer is more desirable.

[0017] As a rubber elastomer used as a component of a pressure sensitive adhesive, specifically for example, a polyisobutylene (for example, trade name:Vistanex made from exon chemistry --) The trade name made from BASUFU : A polyisobutylene available as Oppanol etc., (A-B) a n-A mold elastic polymer (for example, the styrene-butadiene-styrene block copolymer made from shell chemistry (trade name: caliph REXX TR-1101) --) A styrene-isoprene-styrene block copolymer (trade name: caliph REXX TR-1107, caliph REXX TR-1111), the styrene-isoprene-styrene block copolymer (trade name: JSR5000, JSR5100) by Japan Synthetic Rubber Co., Ltd., the styrene-isoprene-styrene block copolymer (trade name: Queen tuck 3421) by Nippon Zeon Co., Ltd., etc. -- etc. -- it is mentioned. these rubber elastomer is independent -- or although it can combine and use, the combination of a polyisobutylene and a styrene-isoprene-styrene block copolymer is desirable. The loadings to the inside of the pressure sensitive adhesive of a rubber elastomer are 5 - 50 % of the weight, are 10 - 40 % of the weight preferably, and are 10 - 30 % of the weight still more preferably.

[0018] As a tackifier of the component of a pressure sensitive adhesive, tackifiers, such as alicycle group saturated hydrocarbon resin (for example, Al Cong P-100 (trade name)), rosin ester (for example, KE-311, KE-100 (trade name), super ester S-100 (trade name)), hydrogenation petroleum system resin (for example, FORARU 105 (trade name)), and terpene system hydrogenation resin (for example, chestnut ARON P-105 (trade name)), are illustrated. The loadings to the inside of a pressure sensitive adhesive are 5 - 50 % of the weight, are 5 - 40 % of the weight preferably, and are 10 - 35 % of the weight still more preferably. As a softener of the component of a pressure sensitive adhesive, softeners, such as a liquid paraffin, polybutene, castor oil, cotton seed oil, palm oil, palm oil, and process oil, are illustrated. The loadings to the inside of a pressure sensitive adhesive are 10 - 70 % of the weight, are 15 - 60 % of the weight preferably, and are 20 - 50 % of the weight still more preferably.

[0019] Moreover, especially as an acrylic binder which can also be used together as a component of a pressure sensitive adhesive with a rubber elastomer, the acrylic-acid (meta) alkyl ester homopolymer of the carbon numbers 4-18 of an alkyl group, a copolymer, or the copolymer of the above-mentioned (meta) acrylic-acid alkyl ester and other functionality monomers is used suitably. As the above-mentioned (meta) acrylic ester, butyl acrylate, isobutyl acrylate, Acrylic-acid hexyl, acrylic-acid octyl,

2-ethylhexyl acrylate, Acrylic-acid iso octyl, acrylic-acid DESHIRU, acrylic-acid isodecyl, Acrylic-acid lauryl, acrylic-acid stearyl, a methyl methacrylate, Ethyl methacrylate, methacrylic-acid butyl, methacrylic-acid isobutyl, 2-ethylhexyl methacrylate, methacrylic-acid iso octyl, methacrylic-acid DESHIRU, methacrylic-acid isodecyl, methacrylic-acid lauryl, stearyl methacrylate, etc. are illustrated. As an example of the above-mentioned functionality monomer, the monomer which has a hydroxyl group, the monomer which has a carboxyl group, the monomer which has an amide group, the monomer which has an amino group, the monomer which has a pyrrolidone ring are mentioned. As a monomer which has a hydroxyl group, hydroxyalkyl (meta) acrylate, such as 2-BIDOROKISHI ethyl (meta) acrylate and hydroxypropyl (meta) acrylate, etc. is illustrated. As a monomer which has a carboxyl group, maleic-acid monoalkyl ester:maleic-acid:fumaric-acid:crotonic acids, such as alpha [, such as an acrylic acid and a methacrylic acid,] and beta-unsaturated-carboxylic-acid:maleic-acid butyl, etc. are illustrated. The copolymerization component as a maleic acid also with the same maleic anhydride is given.

[0020] As a monomer which has an amide group, N-alkoxy methyl (meta) acrylamides, such as alkyl (meta) acrylamide:N-butoxy methylacrylamide, such as acrylamide, dimethyl acrylamide, and diethyl acrylamide, and N-ethoxy methylacrylamide, diacetone acrylamide, etc. are illustrated. Dimethylamino ethyl acrylate etc. is illustrated as a monomer which has an amino group. An N-vinyl-2-pyrrolidone etc. is illustrated as a monomer which has a pyrrolidone ring. The loadings to the inside of the pressure sensitive adhesive layer of these acrylic binders are 0 - 80 % of the weight (in rubber elastomer independent combination, 0 % of the weight is meant), are 5 - 60 % of the weight preferably, and are 10 - 30 % of the weight still more preferably.

[0021] The thickness with a suitable pressure sensitive adhesive layer is 30-300 micrometers, if it is thinner than 30 micrometers, a problem will produce it in adhesion, and emission control may become difficult if thicker than 300 micrometers.

[0022] It becomes equipment for an endermic therapy which possesses the skin safety of the invention in this application, and emission control with the combination of these elastomers, a tackifier, a softener, and/or an acrylic binder.

[0023] Furthermore, a well-known additive can be blended with the pressure sensitive adhesive layer of this invention if needed for preparation of an adhesive property, safety, and stability. Specifically, optimum dose content of the combination of resolvents, such as inorganic bulking agents, such as water absorbing polymers, such as SUMIKAGERU SP-520 (trade name), AKUA keeping 4SH (trade name), ARASOBU 800F (trade name), and SANWETTO 1M-1000MPS (trade name), a zinc oxide, a calcium carbonate, a

titanium dioxide, and silicas, a polyethylene glycol, and crotamiton, etc. is carried out suitably.

[0024] About the film used as a separator layer, it must be required during preservation of equipment to be able to prevent the drugs vaporization from a drugs emission layer etc., and exfoliation removal must be possible for this separator layer in the case of use of equipment. The material of a separator film has aluminum, a cellulose, polyester, polyethylene, usable polypropylene, etc., and may specifically carry out the laminating of these films if needed. Moreover, the front face is processed by silicon or fluorocarbon, or a well-known additive is blended into a liner material, detachability may be adjusted or barrier property may be adjusted. The tongue section for exfoliation can be prepared in a separator so that the handling at the time of exfoliating may become easy. Although seal adhesion needs to be carried out during preservation of equipment about the adhesive property between a drugs emission layer and the separator which covers this, the exfoliation removal of this separator must be able to be carried out on the occasion of use of equipment. Therefore, the adhesive strength between a drugs emission layer and the liner which covers this must be lower than the adhesive strength of a backing material layer and a drugs emission layer.

[0025] Although especially the configuration of equipment is not limited, circular, an ellipse form, a polygon, etc. are raised. The area of equipment has desirable 1cm thing which 2-200cm are in the range of 2. If it will become difficult to remove a separator and to stick equipment on the skin if area is narrower than 2 1cm, and it becomes large from 2 200cm, the feeling of wearing of equipment will worsen. On the other hand about the thickness of equipment, it is desirable in the total thickness of the equipment also containing the separator in a drugs storage tank part that it is the range of 0.1-15mm. Since it is obliged for the amount of administration drugs per drugs emission area to decrease and the durability of drugs emission becomes short when thickness is thinner than 0.1mm, it is not desirable. When thickness is thicker than 15mm, possibility that equipment will exfoliate by sudden actuation of a patient becomes high and is not desirable.

[0026] Thus, a merit since the degree of freedom of a drugs presentation is high as compared with a tape etc., when it is broadly permissible from a viscous low liquefied thing to a viscous liquefied high thing as description of drugs since the obtained equipment for this endermic therapy has the structure where drugs were enclosed between the backing material layer and the drugs emission layer, and designing safety, stability, and effectiveness suitably is large.

[0027] As the manufacture approach of the percutaneous absorption pharmaceutical

preparation of this invention, there is especially no limit and it can be manufactured by the usual approach. For example, after dissolving all the components of a pressure sensitive adhesive layer in organic solvents, such as a hexane, toluene, and ethyl acetate, as the adjustment approach of the drugs emission layer of this invention, it **** to a separator and an organic solvent is removed. A pressure sensitive adhesive layer contrary to a separator side is covered by porosity material, a drugs emission layer is created, that drugs emission layer is cut in a desired configuration, after a backing material layer and heat sealing, the drugs adjusted independently are dropped at a porosity material side, and the equipment for an endermic therapy of this invention is obtained [it judges along with the periphery of this heat sealing, and]. Moreover, about the drugs with which the percutaneous absorption pharmaceutical preparation of this invention is stored, lower alcohol, a moisturizer, water, a stimulus reduction agent, absorption enhancers, and a drug can be prescribed suitably, and can be adjusted with an emulsification test machine (daylight chemical ET-3A mold).

[0028]

[Example] Hereafter, an example and the example of a trial are given and this invention is explained more to a detail. In addition, all the numeric values in an example, the example of a comparison, and the example of reference are weight % criteria.

[0029] Example 1 Presentation of a pressure sensitive adhesive Styrene-isoprene-styrene block copolymer 10.50 Acrylic binder (2-ethylhexyl acrylate / 10.00 vinyl acetate copolymer)

A liquid paraffin 49.30 A tackifier (alicycle group saturated hydrocarbon resin) 20.00 A polyisobutylene 10.00 Dibutylhydroxytoluene 0.20 -- according to the manufacture approach illustrated above, it produced by this formula, and the laminating of the porosity material was carried out, and it cut in desired magnitude and considered as the drugs emission layer.

[0030]

A drugs presentation Ethanol 24.00 The buffer solution 40.00 A glycerol 25.00 Lauryl alcohol 0.50 Glycerol mono-olate 3.00 Sorbitan monolaurate 1.00 Carboxymethylcellulose sodium 3.50 Estradiol 1.00 Acetic-acid norethisterone 0.5g of 2.00 drugs was dropped at the porosity material side, and it heat sealed with the backing material layer, and judged along with the periphery of this heat sealing, and the equipment for an endermic therapy of this invention was obtained.

[0031] Example 2 Presentation of a pressure sensitive adhesive Styrene-isoprene-styrene block copolymer 30.00 Acrylic binder (2-ethylhexyl acrylate / 5.00 ethyl acrylate, and vinyl acetate copolymer)

A liquid paraffin 30.50 A tackifier (alicycle group saturated hydrocarbon resin) 25.00 A polyisobutylene 5.00 A polyethylene glycol 200 4.00 Dibutylhydroxytoluene 0.50 -- according to the above-mentioned manufacture approach, it produced by this formula, and the laminating of the porosity material was carried out, and it cut in desired magnitude and considered as the drugs emission layer.

[0032]

A drugs presentation Ethanol 24.00 The buffer solution 40.50 A polyethylene glycol 300 25.00 Lauryl alcohol 0.50 Glycerol mono-olate 3.00 Sorbitan monolaurate 1.00 Hydroxypropyl methylcellulose 4000 2.00 Estradiol 1.00 Progesterone 0.5g of 3.00 drugs was dropped at the porosity material side, and it heat sealed with the backing material layer, and judged along with the periphery of this heat sealing, and the equipment for an endermic therapy of this invention was obtained.

[0033] Presentation of example 3 pressure sensitive adhesive Styrene-isoprene-styrene block copolymer 15.00 Acrylic binder (2-ethylhexyl acrylate / 11.50 vinyl-pyrrolidone copolymer)

A liquid paraffin 14.50 Tackifier (rosin ester) 35.00 Polyisobutylene 15.00 Crotamiton - 5.00 SANWETTO 1M-1000MPS 3.00 Dibutylhydroxytoluene 1.00 -- according to the above-mentioned manufacture approach, it produced by this formula, and the laminating of the porosity material was carried out, and it cut in desired magnitude and considered as the drugs emission layer.

[0034]

Drugs presentation Ethanol 24.00 Buffer solution 40.50 Polyethylene glycol 400 25.00 Lauryl alcohol 0.50 Glycerol mono-olate 3.00 Sorbitan monolaurate 1.00 Hydroxypropyl methylcellulose 4000 2.00 Estradiol 1.00 Medroxyprogesterone acetate 0.5g of 3.00 drugs was dropped at the porosity material side, and it heat sealed with the backing material layer, and judged along with the periphery of this heat sealing, and the equipment for an endermic therapy of this invention was obtained.

[0035] Presentation of example 4 pressure sensitive adhesive Styrene-isoprene-styrene block copolymer 20.00 Acrylic binder (acrylic acid / acrylic-acid octyl 20.00 copolymer)

A liquid paraffin 34.50 Tackifier (alicycle group saturated hydrocarbon resin) 17.00 Polyisobutylene 8.00 Dibutylhydroxytoluene 0.50 -- according to the above-mentioned manufacture approach, it produced by this formula, and the laminating of the porosity material was carried out, and it cut in desired magnitude and considered as the drugs emission layer.

[0036]

Drugs presentation Ethanol 24.00 Buffer solution 40.00 Polyethylene glycol 300 26.00

Myristyl alcohol 1.00 Glycerol mono-olate 2.00 Hydroxypropyl methylcellulose 4000 2.00 Estradiol 1.00 Acetic-acid norethisterone 0.5g of 4.00 drugs was dropped at the porosity material side, and it heat sealed with the backing material layer, and judged along with the periphery of this heat sealing, and the equipment for an endermic therapy of this invention was obtained.

[0037] Presentation of example 5 pressure sensitive adhesive Styrene-isoprene-styrene block copolymer 25.00 Liquid paraffin 42.00 Tackifier (alicycle group saturated hydrocarbon resin) 20.00 Polyisobutylene 8.00 Polyethylene glycol 200 4.00 Dibutylhydroxytoluene 1.00 -- according to the above-mentioned manufacture approach, it produced by this formula, and the laminating of the porosity material was carried out, and it cut in desired magnitude and considered as the drugs emission layer.

[0038]

Drugs presentation Ethanol 25.00 Buffer solution 41.00 Polyethylene glycol 300 25.00 Myristyl alcohol 1.00 Sorbitan monolaurate 1.00 Hydroxypropyl methylcellulose 4000 2.00 Estradiol 1.00 Progesterone 0.5g of 4.00 drugs was dropped at the porosity material side, and it heat sealed with the backing material layer, and judged along with the periphery of this heat sealing, and the equipment for an endermic therapy of this invention was obtained.

[0039] Presentation of example 6 pressure sensitive adhesive Styrene-isoprene-styrene block copolymer 12.00 Acrylic binder (2-ethylhexyl acrylate / 15.00 vinyl acetate copolymer)

A liquid paraffin 17.80 Tackifier (rosin ester) 33.00 Polyisobutylene 15.00 Crotamiton 5.00 SANWETTO 1M-1000MPS 1.00 Dibutylhydroxytoluene 1.20 -- according to the above-mentioned manufacture approach, it produced by this formula, and the laminating of the porosity material was carried out, and it cut in desired magnitude and considered as the drugs emission layer.

[0040]

Drugs presentation Isopropanol 40.00 Buffer solution 20.00 Polyethylene glycol 400 30.00 Myristyl alcohol 1.00 Sorbitan monolaurate 2.00 BIDOROKISHI propylmethyl cellulose 4000 2.00 Estradiol 1.00 Medroxyprogesterone acetate 0.5g of 4.00 drugs was dropped at the porosity material side, and it heat sealed with the backing material layer, and judged along with the periphery of this heat sealing, and the equipment for an endermic therapy of this invention was obtained.

[0041] Presentation of example 7 pressure sensitive adhesive Styrene-isoprene-styrene block copolymer 12.00 Acrylic binder (2-ethylhexyl acrylate / 5.50 methyl-acrylate copolymer)

A liquid paraffin 23.00 Tackifier (alicycle group saturated hydrocarbon resin) 50.00 Polyisobutylene 8.00 Dibutylhydroxytoluene 1.50 -- according to the above-mentioned manufacture approach, it produced by this formula, and the laminating of the porosity material was carried out, and it cut in desired magnitude and considered as the drugs emission layer.

[0042]

Drugs presentation Ethanol 10.00 Buffer solution 61.00 Polyethylene glycol 400 20.00 Lauryl alcohol 1.00 Sorbitan monolaurate 2.00 PIDOROKISHI propylmethyl cellulose 4000 2.00 Estradiol 1.00 Norethisterone 0.5g of 3.00 drugs was dropped at the porosity material side, and it heat sealed with the backing material layer, and judged along with the periphery of this heat sealing, and the equipment for an endermic therapy of this invention was obtained.

[0043] Presentation of example 8 pressure sensitive adhesive Styrene-isoprene-styrene block copolymer 10.00 Acrylic binder (2-ethylhexyl acrylate / 30.00 vinyl-pyrrolidone copolymer)

A liquid paraffin 29.00 Tackifier (alicycle group saturated hydrocarbon resin) 20.00 Polyisobutylene 10.00 Dibutylhydroxytoluene 1.00 -- according to the above-mentioned manufacture approach, it produced by this formula, and the laminating of the porosity material was carried out, and it cut in desired magnitude and considered as the drugs emission layer.

[0044]

Drugs presentation Ethanol 24.00 Buffer solution 40.00 Glycerol 25.00 Lauryl alcohol 0.50 Glycerol mono-olate 3.00 Sorbitan monolaurate 1.00 Carboxymethylcellulose sodium 3.50 Tulobuterol hydrochloride 0.5g of 3.00 drugs was dropped at the porosity material side, and it heat sealed with the backing material layer, and judged along with the periphery of this heat sealing, and the equipment for an endermic therapy of this invention was obtained.

[0045] Presentation of example 9 pressure sensitive adhesive Styrene-isoprene-styrene block copolymer 30.00 Acrylic binder (2-ethylhexyl acrylate / 10.00 vinyl acetate copolymer)

A liquid paraffin 20.00 Tackifier (alicycle group saturated hydrocarbon resin) 29.50 Polyisobutylene 5.00 Polyethylene glycol 200 5.00 Dibutylhydroxytoluene 0.50 -- according to the above-mentioned manufacture approach, it produced by this formula, and the laminating of the porosity material was carried out, and it cut in desired magnitude and considered as the drugs emission layer.

[0046]

Drugs presentation Ethanol 24.00 Buffer solution 40.50 Polyethylene glycol 300 25.00 Lauryl alcohol 0.50 Glycerol mono-olate 3.00 Sorbitan monolaurate 1.00 Hydroxypropyl methylcellulose 4000 2.00 Indomethacin 0.5g of 4.00 drugs was dropped at the porosity material side, the beat seal was carried out to the backing material layer, it judged along with the periphery of this heat sealing, and the equipment for an endermic therapy of this invention was obtained.

[0047] Presentation of example 10 pressure sensitive adhesive Styrene-isoprene-styrene block copolymer 15.00 Acrylic binder (acrylic acid / acrylic-acid octyl 15.00 copolymer) A liquid paraffin 14.00 Tackifier (alicycle group saturated hydrocarbon resin) 35.00 Polyisobutylene 15.00 Crotamiton 3.00 SANWETTO 1M-1000MPS 2.00 Dibutylhydroxytoluene 1.00 -- according to the above-mentioned manufacture approach, it produced by this formula, and the laminating of the porosity material was carried out, and it cut in desired magnitude and considered as the drugs emission layer.

[0048]

Drugs presentation Ethanol 24.00 Buffer solution 40.50 Polyethylene glycol 400 25.00 Lauryl alcohol 0.50 Glycerol mono-olate 3.00 Sorbitan monolaurate 1.00 Hydroxypropyl methylcellulose 4000 2.00 Estradiol 1.00 Medroxyprogesterone acetate 0.5g of 3.00 drugs was dropped at the porosity material side, and it heat sealed with the backing material layer, and judged along with the periphery of this heat sealing, and the equipment for an endermic therapy of this invention was obtained.

[0049] Presentation of example 11 pressure sensitive adhesive Styrene-isoprene-styrene block copolymer 21.00 Acrylic binder (2-ethylhexyl acrylate / 2.00 vinyl acetate copolymer)

A liquid paraffin 31.00 Tackifier (alicycle group saturated hydrocarbon resin) 16.00 Polyisobutylene 29.00 Dibutylhydroxytoluene 1.00 -- according to the above-mentioned manufacture approach, it produced by this formula, and the laminating of the porosity material was carried out, and it cut in desired magnitude and considered as the drugs emission layer.

[0050]

Drugs presentation Ethanol 20.00 Buffer solution 40.00 Polyethylene glycol 300 30.00 Myristyl alcohol 1.00 Glycerol mono-olate 2.00 Hydroxypropyl methylcellulose 4000 2.00 Oxybutynin hydrochloride 0.5g of 5.00 drugs was dropped at the porosity material side, and it heat sealed with the backing material layer, and judged along with the periphery of this heat sealing, and the equipment for an endermic therapy of this invention was obtained.

[0051] Presentation of example 12 pressure sensitive adhesive Styrene-isoprene-styrene

block copolymer 14.00 Acrylic binder (2-ethylhexyl acrylate / 5.00 vinyl-pyrrolidone copolymer)
liquid paraffin 70.00 Tackifier (alicycle group saturated hydrocarbon resin) 10.00 Dibutylhydroxytoluene 1.00 -- according to the above-mentioned manufacture approach, it produced by this formula, and the laminating of the porosity material was carried out, and it cut in desired magnitude and considered as the drugs emission layer.
[0052]
Drugs presentation Ethanol 24.00 Buffer solution 41.00 Polyethylene glycol 300 25.00 Myristyl alcohol 2.00 Sorbitan monolaurate 1.00 Hydroxypropyl methylcellulose 4000 2.00 Ketoprofen 0.5g of 5.00 drugs was dropped at the porosity material side, and it heat sealed with the backing material layer, and judged along with the periphery of this heat sealing, and the equipment for an endermic therapy of this invention was obtained.
[0053] Presentation of example 13 pressure sensitive adhesive Styrene-isoprene-styrene block copolymer 5.00 Acrylic binder (2-ethylhexyl acrylate / 80.00 methyl-acrylate copolymer)
liquid paraffin 10.00 Tackifier (alicycle group saturated hydrocarbon resin) 5.00 -- according to the above-mentioned manufacture approach, it produced by this formula, and the laminating of the porosity material was carried out, and it cut in desired magnitude and considered as the drugs emission layer.
[0054]
Drugs presentation Isopropanol 40.00 Buffer solution 20.00 Polyethylene glycol 400 30.00 Myristyl alcohol 1.00 Sorbitan monolaurate 2.00 Hydroxypropyl methylcellulose 4000 2.00 Testosterone 0.5g of 5.00 drugs was dropped at the porosity material side, and it heat sealed with the backing material layer, and judged along with the periphery of this heat sealing, and the equipment for an endermic therapy of this invention was obtained.
[0055] Presentation of example 14 pressure sensitive adhesive Styrene-isoprene-styrene block copolymer 20.00 Acrylic binder (2-ethylhexyl acrylate / 13.50 vinyl acetate copolymer)
A liquid paraffin 23.00 Tackifier (alicycle group saturated hydrocarbon resin) 34.00 Polyisobutylene 8.00 Dibutylhydroxytoluene 1.50 -- according to the above-mentioned manufacture approach, it produced by this formula, and the laminating of the porosity material was carried out, and it cut in desired magnitude and considered as the drugs emission layer.
[0056]
Drugs presentation Ethanol 10.00 Buffer solution 61.00 Polyethylene glycol 400 20.00

Lauryl alcohol 1.00 Sorbitan monolaurate 2.00 Hydroxypropyl methylcellulose 4000 2.00 0.5g of norethisterone 4.00 drugs was dropped at the porosity material side, and it heat sealed with the backing material layer, and judged along with the periphery of this heat sealing, and the equipment for an endermic therapy of this invention was obtained.

[0057] The manufacture approach of the example 1 of reference is shown. It **** so that the thickness after drying an acrylic binder (TS-620) on the film with which exfoliation processing was performed may be set to about 50 micrometers, and an organic solvent is removed. On the binder, the laminating of the paper of fine quality of 5cm two round shapes is carried out, and the laminating of the porosity material is further carried out from on the. The paper of fine quality trickles 0.5g of drugs independently adjusted on the porosity material by which the laminating was carried out, and heat seals with a backing material layer. It judges in 20cm two circle, and considers as a test piece so that this heat sealing may take the lead. The manufacture approach of the examples 2-4 of reference is shown. or [covering at a liner, cutting in a desired configuration, and making with a test piece, after dissolving all components in organic solvents, such as a hexane, toluene, and ethyl acetate, ****(ing) to a base material and removing an organic solvent] -- or an after [****] organic solvent is removed on the film with which exfoliation processing was performed, and a sticking-by-pressure imprint is carried out and it considers as a test piece at a suitable base material.

[0058] Example 1 of the example reference of reference Pressure sensitive adhesive Acrylic binder (TS-620: Japanese carbide company make)

A drugs presentation Ethanol 24.00 The buffer solution 40.00 A glycerol 25.00 Lauryl alcohol 0.50 Glycerol mono-olate 3.00 Sorbitan monolaurate 1.00 Carboxymethylcellulose sodium 3.50 It judged in 20cm two circle, and considered as tulobuterol hydrochloride pharmaceutical preparation so that 0.5g of tulobuterol hydrochloride 3.00 drugs might be dropped at a porosity material side and heat sealing of a backing material layer and beat seal Perilla frutescens (L.) Britton var. crispa (Thunb.) Decne. might take the lead.

[0059] The example 2 of reference An acrylic binder 97.00 (trade name TS-620:Japan carbide company make) Solid content Estradiol 0.50 Acetic-acid norethisterone 2.50 -- according to the above-mentioned manufacture approach, it produced by this formula, it cut in desired magnitude, and considered as estradiol and acetic-acid norethisterone mixing pharmaceutical preparation.

[0060] Example 3 of reference Styrene-isoprene-styrene block copolymer 25.00 Polyisobutylene 5.00 Liquid paraffin 42.00 Tackifier (hydrogenation alicycle group hydrocarbon) 25.00 Estradiol 0.50 Acetic-acid norethisterone 2.50 -- according to the

above-mentioned manufacture approach, it produced by this formula, it cut in desired magnitude, and considered as estradiol and acetic-acid norethisterone mixing pharmaceutical preparation.

[0061] Example 4 of reference Silicone binder 92.00 Solid content (trade-name 355Medicaladhesive: Dow Corning make)

crotamiton 5.00 Estradiol 0.50 Acetic-acid norethisterone 2.50 -- according to the above-mentioned manufacture approach, it produced by this formula, it cut in desired magnitude, and considered as estradiol and acetic-acid norethisterone mixing pharmaceutical preparation.

[0062] Example of the example comparison of comparison 1 Estraderm TTS (Ciba-Geigy make)

[0063] Example of comparison 2 Nitroderm TTS (Ciba-Geigy make)

[0064] An adhesion test and skin irritation study were performed in the test piece, the example 1 of reference, and 2 lists of an example of the example trial of trial 1. adhesion test example by the following technique per test piece of the example of a comparison. It evaluated by sticking a test piece on 20 test subjects' (healthy people, male) overarm section, and sticking for 72 hours. The result is shown in Tables 1 and 2. an adhesion test -- ** **: -- 03/4 exfoliation: -- 11/2 exfoliation: -- 21/4 exfoliation: -- 3 edge exfoliation: -- with no 4 exfoliation : It evaluated in five steps of 5 and the average of a test subject was shown as a score all over Table 1. In the example, those without exfoliation were almost the case to that (score 3.4) in which 1/2 or more ****s was accepted in pasting of 72 hours more than the moiety in the example of a comparison (score 1.7), and 1/4 exfoliation was accepted more than the moiety in the example 1 of reference so that clearly also from the score shown all over Table 1 (scores 4.2-5.0). moreover, with [skin irritation study] no erythema : 0 -- very slight erythema : 1 -- clear erythema : Whenever [middle / of two], thru/or strong erythema : Four steps of evaluations of 3 were performed and the average of a test subject was shown as a score all over Table 2. More than the moiety of the examples 1 and 2 of reference and the example of a comparison was below very slight erythema in the example to that (scores 1.7-2.8) which accepted clear erythema so that clearly also from the score in Table 2 (scores 0.0-0.3).

[0065]

[Table 1]

[0066]

[Table 2]

[0067] 50 degrees of each test piece of an example of trial 2. stability test example and the example 1 of reference were saved for C.2 months, and it checked about weight change of each test piece and the leakage of drugs. It x Swerved from the test piece with 10% or more of weight change, and except was taken as O. what has adhesion of drugs at a liner in case a liner is removed about drugs leakage -- x -- it considered as O except it. A result is shown in Table 3. In the example, all were O to weight change and the leakage of drugs being x in the example 1 of reference.

[0068]

[Table 3]

[0069] After sticking the test piece of an example of trial 3. cohesive-force trial example, and the example of a comparison on the stainless plate, respectively and leaving it for a while, the test piece was slowly exfoliated with the finger and condition observation in the case of the exfoliation was performed. What that to which some in which what has the binder remainder in a stainless plate does not x Remain have ****** in O pan does not x Have evaluated by considering as O. The result is shown in Table 4. In the example of a comparison, ****** was accepted in all to the binder remainder and ****** not having been accepted at all in the example.

[0070]

[Table 4]

[0071] The emission trial was performed by the rotating-cylinder method per test piece of the example of example of trial 4. emission test reference, and an example. As a test condition, it carried out by 32.0 **0.5-degreeC and cylinder rotational frequency 50rpm whenever [900ml / of test fluid /, and trial solution temperature]. A result is shown in

drawing 3 and 4. The thing of the example of reference started, it went up rapidly, and it turned out to falling in the second half that the thing of the example of this invention is a thing of a fixed burst size (controlled). The thing of an example showed the pattern by which emission control was carried out to the test piece of the example of reference serving as a primary emission by which emission control is not carried out, and it was shown that the equipment for an endermic therapy of this invention emits the drug of an amount effective in a therapy correctly and certainly.

[0072]

[Effect of the Invention] With the equipment for an endermic therapy of this invention, the increment in the skin stimulus in accordance with being bulky by arranging the adhesive fall and pressure sensitive adhesive layer by the interaction with drugs around during preservation of equipment can be abolished. Moreover, it can apply the drugs of a quantum to a patient correctly and certainly beforehand on the occasion of use while the drugs emission side is sealed during preservation of equipment, and it cancels this sealing performance on the occasion of use of equipment and abolishes the drugs loss under preservation substantially, since this invention is equipment with which the drug of an amount effective in a therapy passes a drugs emission layer from the storage tank of drugs liquid, and is supplied to a skin front face.

[Translation done.]

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TECHNICAL FIELD

[Field of the Invention] This invention relates to the field of endermic medication. It is related with the equipment for an endermic therapy which is equipment for an endermic therapy which made it possible to control the exsorption from the drug storage tank of the liquefied drugs under preservation of equipment, and is characterized by the drugs of a quantum being certainly [correctly and] applicable to a patient beforehand by carrying out the laminating of the drugs emission control pressure sensitive adhesive to a detail more in a drug release side.

[Translation done.]

PRIOR ART

[Description of the Prior Art] In the field of an endermic therapy, equipments for an endermic therapy, such as Estraderm (trade name) and nitro DAMU (trade name), are already developed and sold now. However, as for these equipments, the adhesion of the equipment to the skin may fall during preservation by the interaction with drugs. Such an adhesive fall can pose a problem fatal to patches.
[0003] Moreover, some equipments for an endermic therapy with which the emission surface part of drugs and the pressure sensitive adhesive layer in connection with adhesion on the skin were separated are also proposed. For example, the example which made between a drugs storage tank and the adhesives which exist in the periphery divide into JP,61-265150,A with a circumferencial direction seal is indicated. The equipment for an endermic therapy shown in examples, such as JP,60-63344,U, JP,62-182942,U, JP,62-195326,A, JP,1-224312,A, JP,4-46592,B, a ****** No. 503252 [six to] official report, JP,2-1283,A, and JP,62-212320,A, is also common in JP,61-265150,A in that the pressure sensitive adhesive layer of the perimeter of a drugs emission side and the interaction of a drugs storage tank are cut off. However, if a pressure sensitive adhesive layer which is seen by these examples is arranged around a drugs emission side, the whole equipment will be bulky and the adhesion to the skin will fall. Then, in order to raise adhesion, or it enlarges area of a pressure sensitive adhesive layer, adhesive strength will be raised and we are anxious about the increment in a skin stimulus.
[0004] The estradiol contained in estrogen on the other hand when it says about a drug is secreted from the ovary at the stage when it can reproduce female. Therefore, the woman before and behind a menopause mainly causes lack of estradiol, and symptoms, such as menopausal disorders and an emmeniopathy, produce her. Although the cure by oral agent administration etc. is performed for the purpose which improves these symptoms now, since alimentary canals, liver, etc., such as the stomach and intestines, are metabolized quickly and inactivation is carried out, in order to expect sufficient drug effect manifestation, high-dose estradiol must be taken. Moreover, there is a possibility that manifestation nature, such as a side effect, may increase for a high dose. Then, the attempt with which is going to lessen the metabolic turnover of estradiol by dermal administration, and tends to be made to reach into blood, and it is going to present a therapy is made. For example, in JP,6-51623,B and a ****** No. 501386 [three to] official report, hormone, such as estradiol, is made to enclose into the gel of ethanol, and it is proposed about the reservoir mold pharmaceutical preparation which carries out emission control with the control film. However, the skin stimulus by ethanol occurs frequently and these have the problem that the cohesive force of a binder declines by the interaction with a drug solution. Examination which is made to absorb from transderma the corpus luteal hormone which is other hormone on the other hand, and suppresses the side effect in estradiol administration is also made. For example, in the ****** No. 500740 [two to] official report, estrogen and the percutaneous absorption pharmaceutical preparation containing the progestogen are proposed in a silicone system polymer basis, and the gel pharmaceutical preparation which contains estrogen in an acrylic ester system polymer basis is proposed by JP,3-220121,A. However, in these pharmaceutical preparation, when 17-beta-estradiol, norethisterone, etc. were used, it had the fault that sustained-release was not enough.

Moreover, the percutaneous absorption pharmaceutical preparation which uses estradiol and corpus luteal hormone as a drug effect component at JP,4-342532,A, and uses as a principal component the acrylic binder which consists of 2-ethylhexyl acrylate and an N-vinyl-2-pyrrolidone as a binder is proposed. However, drug release nature is low, and the stimulus to the skin of an acrylic binder is strong, and it is intolerable to long-term repetitive administration. Moreover, the pharmaceutical preparation by which these emission is controlled has a possibility that blood drug concentration may rise at a stretch by the rapid standup of initial emission, and the manifestation of a side effect may increase.

[Translation done.]

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EFFECT OF THE INVENTION

[Effect of the Invention] With the equipment for an endermic therapy of this invention, the increment in the skin stimulus in accordance with being bulky by arranging the adhesive fall and pressure sensitive adhesive layer by the interaction with drugs around during preservation of equipment can be abolished. Moreover, it can apply the drugs of a quantum to a patient correctly and certainly beforehand on the occasion of use while the drugs emission side is sealed during preservation of equipment, and it cancels this sealing performance on the occasion of use of equipment and abolishes the drugs loss under preservation substantially, since this invention is equipment with which the drug of an amount effective in a therapy passes a drugs emission layer from the storage tank of drugs liquid, and is supplied to a skin front face.

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TECHNICAL PROBLEM

[Problem(s) to be Solved by the Invention] The technical problem which this invention tends to solve is a thing which depend the adhesive fall and pressure sensitive adhesive layer by the interaction with drugs on arranging around during preservation of equipment and for which the increment in the skin stimulus in accordance with being bulky is abolished. Moreover, although this invention relates to the equipment with which the drug of an amount effective in a therapy passes a drugs emission layer from the storage tank of drugs liquid, and is supplied to a skin front face While the drugs emission side is sealed during preservation of equipment, canceling this sealing performance on the occasion of use of equipment and abolishing the drugs loss under preservation substantially, it is going to offer the equipment for an endermic therapy which can apply the drugs of a quantum to a patient correctly and certainly beforehand on the occasion of use.

[Translation done.]

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MEANS

[Means for Solving the Problem] this invention persons found out that exsorption could be prevented, controlling emission of drugs by using the drugs emission layer which consists of a pressure sensitive adhesive layer which can control emission of a drug in the equipment for an endermic therapy as a result of repeating research wholeheartedly, in order to solve the above-mentioned technical problem. That is, while being able to prevent the increment in a skin stimulus which depends for acquiring good adhesion by the equipment for an endermic therapy of this invention which has the drugs emission layer which consists of a pressure sensitive adhesive layer which can control emission of a drug, and being bulky, exsorption of drugs prevents during preservation, and after sticking this equipment to the patient skin, it becomes that it is possible in the drugs of an amount effective in a therapy being emitted from this equipment correctly and certainly. therefore, this invention -- 1 -- it is in offering the equipment for an endermic therapy which planned emission control of the drugs by simple structure, improvement in the preservation stability of two drugs, reduction of 3 skin irritation, good adhesion to the 4 skin, and high cohesive force of five pressure sensitive adhesives.
[0007] This invention (A) Backing material layer of drugs nontransparent nature (B) Drugs storage reservoir which the drug of an amount effective in a therapy contained between the backing material layer and the drugs emission layer (C) It is related with the equipment for an endermic therapy which has the drugs emission layer which consists of a pressure sensitive adhesive layer which can control emission of a drug, and at least three layers which become more. The equipment for an endermic therapy of this invention can also have the separator layer which can be exfoliated on the occasion of use of equipment on the outside of the above mentioned drugs emission layer. Moreover, the drugs emission layer which controls emission of the drugs of this invention can also include the drugs permeability film (henceforth a porous layer) other than a pressure sensitive adhesive layer. This invention is more at a detail to offer the equipment for an endermic therapy which has a drugs emission layer containing the pressure sensitive adhesive layer which can control emission of the drug which consists of a pressure sensitive adhesive containing a rubber elastomer, a tackifier, and a softener, or a pressure sensitive adhesive which makes it come further to contain an acrylic binder for these components. Furthermore, the pressure sensitive adhesive layer of this invention applies the above mentioned pressure sensitive adhesive to a detail all over a drugs emission layer.
[0008] This invention is explained concretely below. What has the layer structure shown in drawing 1 as one gestalt of the equipment for an endermic therapy of this invention can be mentioned. The liquefied drugs containing the drug effect component of an amount with the thing of drawing 1 effective in a therapy are enclosed in drugs storage reservoir ** between backing material layer ** and porosity material ** of a drugs permeability film. The laminating of the pressure sensitive adhesive layer ** is carried out to the outer layer of porosity material **, and separator ** for sealing drugs is covered. On the occasion of use of this equipment, exfoliation removal of this separator ** is carried out. Drawing 2 is drawing which looked at the condition of equipment of having removed separator ** of the equipment for an endermic therapy of this invention shown in drawing 1 , from the skin side. Moreover, press layer ** is pressed depth along with the periphery of an effective emission side in the part which gave the drug

transparency film and the seal of backing material for seal of drugs storage reservoir **. Since drugs do not store between separator **s by pressure sensitive adhesive layer **, the drugs loss accompanying removal of separator ** is lost. When this equipment is applied to the patient skin, it becomes possible from a drugs emission layer to emit drugs.
[0009] If the drug used as an active principle needs to have percutaneous absorption by the activity matter physiologically, there will be especially no limit. Moreover, after percutaneous absorption of the drug of this invention is carried out, it may be the so-called prodrug as shows bioactive. For example, as an active principle, as estrogen, as estradiol, the estradiol dipropionate, estrogens conjugated, mestranol, estriol, equilin, equilenins, or those derivatives, although estradiol benzoate, ethinylestradiol, estradiol valerate and estriol propionate, estriol tripropionate, estriol acetate benzoate, etc. are mentioned, estradiol is used especially in this invention. Moreover, as corpus luteal hormone, although progesterone, hydroxyprogesterone caproate, medroxyprogesterone acetate, dydrogesterone, chlormadinone acetate, the ethisterone, the dimethisterone, norethisterone, acetic-acid norethisterone, enanthic acid norethisterone, acetic-acid ethynodiol, the megestrol acetate, or allylestrenol is mentioned, especially in this invention, acetic-acid norethisterone is desirable.
[0010] in addition, as a drug effective in the equipment for this endermic therapy for example, a coronary vasodilator (example: -- nitroglycerin and isosorbide dinitrate --) Diltiazem hydrochloride, nifedipine, nicorandil, nitrendipine, etc., Local anesthetic (example: lidocaine, benzocaine, procaine hydrochloride, tetracaine, etc.), a skeletal muscle relaxant (INAPERIZON example: -- eperisone, teaser NIJIN, and tolperisone --) anti-hypertension agents (example: -- clonidine --), such as pridinol and a dantrolene Reserpine, guanethidine sulfate, EHONIJIPIN, pindolol, bopindolol malonate, painkillers (example: -- morphine and buprenorphine hydrochloride --), such as captopril and delapril Fentanyl citrate, pentazocine, eptazocine hydrobromide, etc., a dysuria therapy agent (hydrochloric acid CHIRORIJIN [and] example: -- clenbuterol hydrochloride --) [acetic acid] antiepiletic agents (example: -- nitrazepam --), such as oxybutynin hydrochloride and hula BOKISATO anti-Parkinson's disease agents (example: -- the chlorzoxazone --), such as meprobamate antiallergic agents (example: -- tranilast and azelastine --), such as REPODOPA Ketotifen, mequitazine, ibudilast, oxatomide, EMEDASUCHIN, etc., a central nervous system acting drug (example: -- chlorpromazine, nitrazepam, and diazepam --) antiphlogistic sedative drugs (example: -- indomethacin --), such as reserpine and imipramine Ketoprofen, diclofenac, ketorolac, felbinac, flurbiprofen, Loxoprofen, tenidap, ETODORAGU, indometacin farnesil, etc., smoking cessation aids (example: nicotine) and an antiemetic drug (example: -- haloperidol and timiperone --) prostagladins (example :P [1] GE and PGF2alpha --), such as benperidol, FURoROPAMIDO, and FANIZON PGE2, PGI2 grade, an anti-dizziness agent (example: diphenidol, betahistine, etc.), a sympathetic nerve stimulant (example: -- salbutamol sulfate, tulobuterol hydrochloride, and procaterol hydrochloride --) immunity modifiers (example: -- LPS and auranofin --), such as a hydrochloric-acid MAPUTE roll The hormone drug of polypeptide systems, such as lobenzarit, (LH-RH, TRH, etc.), The drug of the class of anti-estrogen agents (example: tomoxifen, a hydrochloric acid a fado ROZORU etc.), other hormone drugs (example: testosterone etc.), etc. can be used, and although it changes with combination purposes, 0.1 - 10% of the weight of loadings are usually preferably used to drugs as an amount effective in a therapy. Moreover, when un-arranging according to an interaction does not arise, two or more kinds of concomitant use is also possible for these drugs if needed.
[0011] As for the drug which this invention described above, it is desirable to add other components and to make it store in a drugs storage reservoir as liquefied drugs. As a presentation of the basis for considering as the liquefied drugs of the equipment for an endermic therapy of this invention, the 10 - 40-% of the weight range has [the blending ratio of coal of lower alcohol] the desirable blending ratio of coal of a water component 20 to 70% of the weight. The blending ratio of coal of the fatty alcohol which is absorption enhancers has 0.1 - 10% of the weight of desirable within the limits. The glycerol of a moisturizer or the blending ratio of coal of a polyethylene glycol has 20 - 40% of the weight of the desirable range. Finally, the blending ratio of coal of the glycerol mono-olate of a stimulus reduction agent, glycerine monolaurate, or those mixture has 1 - 10% of the weight of the desirable range, and is suitably prescribed as each of

these bases are also in the range of each blending ratio of coal. Moreover, these can add a gelling agent if needed.
[0012] As a gelling agent, proper gelling agents, such as a carboxy vinyl polymerization object, sodium polyacrylate, a polyvinyl pyrrolidone, hydroxypropyl methylcellulose, hydroxyethyl cellulose, hydroxypropylcellulose, methyl cellulose, and a carboxymethyl cellulose, are illustrated. Furthermore, additives, such as an ultraviolet ray absorbent, an anti-oxidant, and antiseptics, may be added if needed. For example, P-aminobenzoic-acid derivative well-known as an ultraviolet ray absorbent, an anthranilic-acid derivative, salicylic acid derivatives, a coumarin derivative, an amino acid derivative, a benzotriazol derivative, a tetrazole derivative, an imidazoline derivative, a pyrimidine derivative, a dioxane derivative, a furan derivative, a pyrone derivative, a camphor derivative, a nucleic-acid derivative, an allantoin derivative, a nicotinic-acid derivative, a shikonin, or vitamin 6 derivative is illustrated, and benzophenone derivatives, such as a 2-hydroxy-4-methoxybenzophenone derivative, are used especially suitably. As an anti-oxidant, proper anti-oxidants, such as an ascorbic acid, stearic acid ester, sodium ascorbate, tocopherols (d bodies, such as alpha-tocopherol, beta-tocopherol, gamma-tocopherol, and delta-tocopherol, l bodies, dl object) and these ester derivatives, the NORUJIHIDOROGUASE retinoic acid, dibutylhydroxytoluene, burylhydroxyanisole, tert-butyl BIDOROKISHINON, gallate (ester, such as ethyl, propyl, and isoamyl), and 1-oxo--3-methyl-4-isopropylbenzene, are illustrated.
[0013] Next, a backing material layer is described. The film used as a backing material layer needs to be excellent in the so-called barrier property for prevention of the exsorption and vaporization of drugs, and needs to have the property of being able to paste up easily with the porosity material of a drugs emission material layer. Moreover, it is desirable that there is moderate flexibility at the time of sticking equipment on the skin. Although especially limitation will not be carried out as a material of a backing material film if it has the above-mentioned conditions, aluminum, an ethylene vinyl acetate copolymer or its saponification object, cellulose acetate, a cellulose, nylon, polyester, polyethylene, a polyvinylidene chloride, a polycarbonate, polyvinyl alcohol, polypropylene, etc. are specifically raised as an example. These materials can carry out the laminating of what made the shape of a film or was made paper and blanket-like if needed to a film, can process it in the shape of a laminated film, or can process the vacuum plating of aluminium, ceramic vacuum evaporationo, etc., and can improve barrier property, an adhesive property with a drugs emission material layer, etc.
[0014] Here, an example of a presentation of the desirable drugs which can be used for this invention is shown. As absorption enhancers used by this invention, the fatty acid, fatty alcohol, or fatty acid ester to carbon numbers 7-20 shows sorbefacient [with desirable especially especially expensive lauryl alcohol and myristyl alcohol], and the skin has stimulative [comparatively very little]. Moreover, as a moisturizer, a sorbitol, a polyethylene glycol, diglycerol, propylene glycol, a butylene glycol, dipropylene glycol, sodium pyrrolidone carboxylate, ethyl carbitol, D-xylitol, a glycerol, and hyaluronic acid are desirable, and a glycerol or a polyethylene glycol is desirable especially in it. About a water component, the buffer solution is desirable and the MAKKURU vein buffer solution which is especially the broader-based buffer solution is desirable. As a stimulus reduction agent, fatty acid ester, sorbitol fatty acid ester, or its mixture is desirable. Especially as lower alcohol, ethanol or isopropanol is desirable.
[0015] As a material which forms a drugs permeability film, it is porosity material, and an ethylene vinyl acetate copolymer, a cellulose, cellulose acetate, polyester, polyethylene, polypropylene, etc. are specifically raised. A drugs permeability film can consist of one sort of the macromolecule of the shape of the shape of the shape of a fine porosity film which has permeability, and paper, blanket-like, or sponge, or two sorts or more. About porosity material, it is desirable that it is the range whose gar rhe type permeability is 10-500sec / 100 cc.
[0016] The pressure sensitive adhesive layers which can control emission of a drug are conditions with required having sufficient adhesive strength for making equipment adhere to the skin. Moreover, excelling in the safety to the skin is desirable. As a pressure sensitive adhesive layer of this invention, the thing using the pressure sensitive adhesive containing a rubber elastomer, a tackifier, and a softener or the pressure sensitive adhesive which makes these components come to contain an acrylic binder further is desirable. As for the pressure sensitive

adhesive layer of this invention, what applied the above mentioned pressure sensitive adhesive all over the drugs emission layer is more desirable.

[0017] As a rubber elastomer used as a component of a pressure sensitive adhesive, specifically for example, a polyisobutylene (for example, trade name:Vistanex made from exon chemistry --) The trade name made from BASUFU : A polyisobutylene available as Oppanol etc., (A-B) a n-A mold elastic polymer (for example, the styrene-butadiene-styrene block copolymer made from shell chemistry (trade name: caliph REXX TR-1101) --) A styrene-isoprene-styrene block copolymer (trade name: caliph REXX TR-1107, caliph REXX TR-1111), the styrene-isoprene-styrene block copolymer (trade name: JSR5000, JSR5100) by Japan Synthetic Rubber Co., Ltd., the styrene-isoprene-styrene block copolymer (trade name: Queen tuck 3421) by Nippon Zeon Co., Ltd., etc. -- etc. -- it is mentioned. these rubber elastomer is independent -- or although it can combine and use, the combination of a polyisobutylene and a styrene-isoprene-styrene block copolymer is desirable. The loadings to the inside of the pressure sensitive adhesive of a rubber elastomer are 5 - 50 % of the weight, are 10 - 40 % of the weight preferably, and are 10 - 30 % of the weight still more preferably.

[0018] As a tackifier of the component of a pressure sensitive adhesive, tackifiers, such as alicycle group saturated hydrocarbon resin (for example, Al Cong P-100 (trade name)), rosin ester (for example, KE-311, KE-100 (trade name), super ester S-100 (trade name)), hydrogenation petroleum system resin (for example, FORARU 105 (trade name)), and terpene system hydrogenation resin (for example, chestnut ARON P-105 (trade name)), are illustrated. The loadings to the inside of a pressure sensitive adhesive are 5 - 50 % of the weight, are 5 - 40 % of the weight preferably, and are 10 - 35 % of the weight still more preferably. As a softener of the component of a pressure sensitive adhesive, softeners, such as a liquid paraffin, polybutene, castor oil, cotton seed oil, palm oil, palm oil, and process oil, are illustrated. The loadings to the inside of a pressure sensitive adhesive are 10 - 70 % of the weight, are 15 - 60 % of the weight preferably, and are 20 - 50 % of the weight still more preferably.

[0019] Moreover, especially as an acrylic binder which can also be used together as a component of a pressure sensitive adhesive with a rubber elastomer, the acrylic-acid (meta) alkyl ester homopolymer of the carbon numbers 4-18 of an alkyl group, a copolymer, or the copolymer of the above-mentioned (meta) acrylic-acid alkyl ester and other functionality monomers is used suitably. As the above-mentioned (meta) acrylic ester, butyl acrylate, isobutyl acrylate, Acrylic-acid hexyl, acrylic-acid octyl, 2-ethylhexyl acrylate, Acrylic-acid iso octyl, acrylic-acid DESHIRU, acrylic-acid isodecyl, Acrylic-acid lauryl, acrylic-acid stearyl, a methyl methacrylate, Ethyl methacrylate, methacrylic-acid butyl, methacrylic-acid isobutyl, 2-ethylhexyl methacrylate, methacrylic-acid iso octyl, methacrylic-acid DESHIRU, methacrylic-acid isodecyl, methacrylic-acid lauryl, stearyl methacrylate, etc. are illustrated. As an example of the above-mentioned functionality monomer, the monomer which has a hydroxyl group, the monomer which has a carboxyl group, the monomer which has an amide group, the monomer which has an amino group, the monomer which has a pyrrolidone ring are mentioned. As a monomer which has a hydroxyl group, hydroxyalkyl (meta) acrylate, such as 2-BIDOROKISHI ethyl (meta) acrylate and hydroxypropyl (meta) acrylate, etc. is illustrated. As a monomer which has a carboxyl group, maleic-acid monoalkyl ester:maleic-acid:fumaric-acid:crotonic acids, such as alpha [, such as an acrylic acid and a methacrylic acid,] and beta-unsaturated-carboxylic-acid:maleic-acid butyl, etc. are illustrated. The copolymerization component as a maleic acid also with the same maleic anhydride is given.

[0020] As a monomer which has an amide group, N-alkoxy methyl (meta) acrylamides, such as alkyl (meta) acrylamide:N-butoxy methylacrylamide, such as acrylamide, dimethyl acrylamide, and diethyl acrylamide, and N-ethoxy methylacrylamide, diacetone acrylamide, etc. are illustrated. Dimethylamino ethyl acrylate etc. is illustrated as a monomer which has an amino group. An N-vinyl-2-pyrrolidone etc. is illustrated as a monomer which has a pyrrolidone ring. The loadings to the inside of the pressure sensitive adhesive layer of these acrylic binders are 0 - 80 % of the weight (in rubber elastomer independent combination, 0 % of the weight is meant), are 5 - 60 % of the weight preferably, and are 10 - 30 % of the weight still more preferably.

[0021] The thickness with a suitable pressure sensitive adhesive layer is 30-300 micrometers, if

it is thinner than 30 micrometers, a problem will produce it in adhesion, and emission control may become difficult if thicker than 300 micrometers.
[0022] It becomes equipment for an endermic therapy which possesses the skin safety of the invention in this application, and emission control with the combination of these elastomers, a tackifier, a softener, and/or an acrylic binder.
[0023] Furthermore, a well-known additive can be blended with the pressure sensitive adhesive layer of this invention if needed for preparation of an adhesive property, safety, and stability. Specifically, optimum dose content of the combination of resolvents, such as inorganic bulking agents, such as water absorbing polymers, such as SUMIKAGERU SP-520 (trade name), AKUA keeping 4SH (trade name), ARASOBU 800F (trade name), and SANWETTO 1M-1000MPS (trade name), a zinc oxide, a calcium carbonate, a titanium dioxide, and silicas, a polyethylene glycol, and crotamiton, etc. is carried out suitably.
[0024] About the film used as a separator layer, it must be required during preservation of equipment to be able to prevent the drugs vaporization from a drugs emission layer etc., and exfoliation removal must be possible for this separator layer in the case of use of equipment. The material of a separator film has aluminum, a cellulose, polyester, polyethylene, usable polypropylene, etc., and may specifically carry out the laminating of these films if needed. Moreover, the front face is processed by silicon or fluorocarbon, or a well-known additive is blended into a liner material, detachability may be adjusted or barrier property may be adjusted. The tongue section for exfoliation can be prepared in a separator so that the handling at the time of exfoliating may become easy. Although seal adhesion needs to be carried out during preservation of equipment about the adhesive property between a drugs emission layer and the separator which covers this, the exfoliation removal of this separator must be able to be carried out on the occasion of use of equipment. Therefore, the adhesive strength between a drugs emission layer and the liner which covers this must be lower than the adhesive strength of a backing material layer and a drugs emission layer.
[0025] Although especially the configuration of equipment is not limited, circular, an ellipse form, a polygon, etc. are raised. The area of equipment has desirable 1cm thing which 2-200cm are in the range of 2. If it will become difficult to remove a separator and to stick equipment on the skin if area is narrower than 2 1cm, and it becomes large from 2 200cm, the feeling of wearing of equipment will worsen. On the other hand about the thickness of equipment, it is desirable in the total thickness of the equipment also containing the separator in a drugs storage tank part that it is the range of 0.1-15mm. Since it is obliged for the amount of administration drugs per drugs emission area to decrease and the durability of drugs emission becomes short when thickness is thinner than 0.1mm, it is not desirable. When thickness is thicker than 15mm, possibility that equipment will exfoliate by sudden actuation of a patient becomes high and is not desirable.
[0026] Thus, a merit since the degree of freedom of a drugs presentation is high as compared with a tape etc., when it is broadly permissible from a viscous low liquefied thing to a viscous liquefied high thing as description of drugs since the obtained equipment for this endermic therapy has the structure where drugs were enclosed between the backing material layer and the drugs emission layer, and designing safety, stability, and effectiveness suitably is large.
[0027] As the manufacture approach of the percutaneous absorption pharmaceutical preparation of this invention, there is especially no limit and it can be manufactured by the usual approach. For example, after dissolving all the components of a pressure sensitive adhesive layer in organic solvents, such as a hexane, toluene, and ethyl acetate, as the adjustment approach of the drugs emission layer of this invention, it **** to a separator and an organic solvent is removed. A pressure sensitive adhesive layer contrary to a separator side is covered by porosity material, a drugs emission layer is created, that drugs emission layer is cut in a desired configuration, after a backing material layer and heat sealing, the drugs adjusted independently are dropped at a porosity material side, and the equipment for an endermic therapy of this invention is obtained [it judges along with the periphery of this heat sealing, and]. Moreover, about the drugs with which the percutaneous absorption pharmaceutical preparation of this invention is stored, lower alcohol, a moisturizer, water, a stimulus reduction agent, absorption enhancers, and a drug can be prescribed suitably, and can be adjusted with an emulsification test machine (daylight

chemical ET-3A mold).

[Translation done.]